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SERUM PROTEINS IN KWASHIORKOR

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Although it is now generally accepted that kwashiorkor is a protein-deficiency disease, certain aspects of the condition which have so far not been studied appeared worthy of investigation. Among these aspects are:

1. The detailed pattern of the serum proteins in kwashiorkor as portrayed by starch-gel electrophoresis.
2. The day-to-day changes in pattern observed during relapse and recovery.
3. The proteins of the interstitial oedema fluid.
4. The relationships, if discernible, between these biochemical observations and the clinical picture.

An account is given of the results of investigations along these lines in this preliminary report.

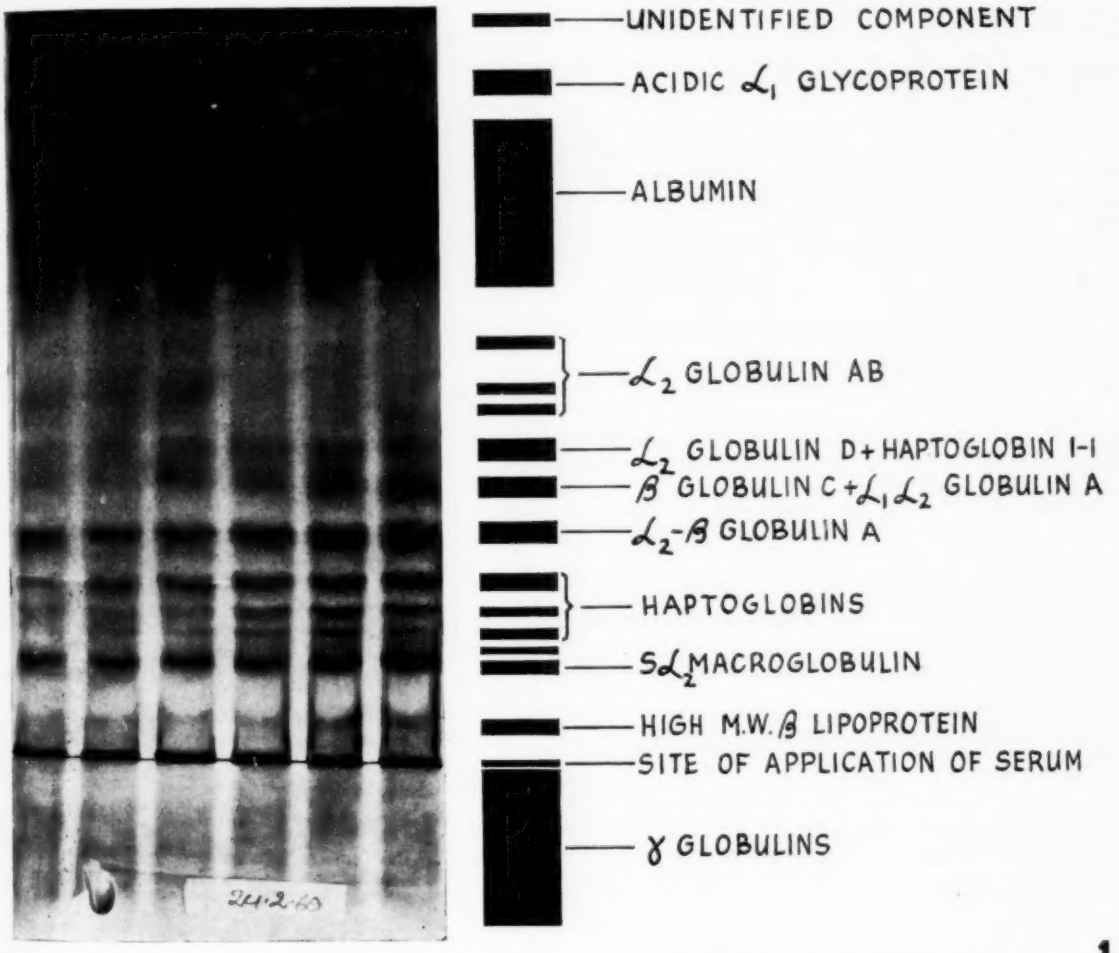

Fig. 1. Serum proteins in the first 6 days of treatment illustrating, in this case, a rapid increase in the concentration of the haptoglobin fractions.

METHODS

Eleven children suffering from kwashiorkor were studied. Treatment was as follows: Each child was given half-strength Darrow's solution and 2·5% glucose by mouth for 24 hours, followed by ½-cream skimmed milk for 2 days and full cream for another 2 days; 2·5 oz. of each of these foods being given daily per lb. of body weight. A mixed diet was given from the 10th day. Vitamins and potassium supplements were added and broad-spectrum antibiotics administered to control infection. Cortisone was given to 2 children to counteract a state of collapse.

Blood was collected from the 11 subjects in tubes either from finger or heel pricks. The serum was separated immediately and stored at 4°C until it could be studied. Sera were examined spectroscopically for evidence of haemolysis. Grossly haemolysed sera were discarded; those containing traces only of haemoglobin were examined, the extent of haemolysis being recorded.

In 2 cases oedema fluid was collected from the foot for investigation. Sera were collected daily, or sometimes specimens were obtained on alternate days. Total serum proteins were measured by the standard biuret procedure, and the detailed fractional distribution of the proteins was examined by vertical starch-gel electrophoresis.[1]

RESULTS

Serum Proteins

The concentration of total proteins on admission ranged between 2·76 and 4·15 g. with a mean value of 3·58 g. per 100 ml. The albumin varied between 1·0 and 1·98 g. with a mean value of 1·57 g. per 100 ml.

The electrophoretic pattern on admission showed that some fractions were little depleted even at the gravest stage of the illness. These were the γ globulins, α_1 acidic glycoprotein, α_2 globulin AB, and the S α_2 macro-molecular globulin.

Recovery changes were evident in the appearance of bands not initially present or by an increase in intensity of a band. Alterations of this nature appeared as early as the 3rd day after admission, more usually from the 5th to the 7th day, but in one child they were delayed until the 10th day.

The sequence of changes in the serum-protein pattern was variable:

1. In 2 cases the earliest increase was apparent in serum albumin closely followed by β globulin C.
2. In some haptoglobins appeared first followed by β globulin C and serum albumin (Fig. 1).
3. In others, β globulin C was the first to appear.
4. In 1 case the haptoglobins were still not normal 8 weeks after admission.
5. Bands appeared suddenly in some cases whilst in others a transient appearance of a band might precede by some days the return to an established normal pattern.

It is clear that there is no consistent sequence by which the various serum proteins reappear.

Proteins of Oedema Fluid

Oedema fluid collected from 2 cases on 3 separate occasions was found to have a total protein varying between 0·46 and 0·5 g. per 100 ml. Electrophoretic separation showed that most of the protein was albumin. Loss of weight associated with disappearance of oedema in 1 child indicated that the oedema fluid present weighed 5 lb.; the total protein contained in the oedema fluid must therefore have been approximately 12 g. The return of even part of this protein into the circulating blood could have an appreciable effect on the recovery pattern of the serum proteins, a factor until now apparently not recognized.

CORRELATION OF BIOCHEMICAL WITH CLINICAL OBSERVATIONS

1. Clinical signs of recovery were invariably accompanied by improvement in the electrophoretic pattern detailed above. However, in some cases, despite a trend towards normal in the pattern, death ensued.
2. Children assessed as being mildly affected, because they could stand or walk, recovered more rapidly both clinically and also biochemically (as judged by the concentrations of various proteins present in the serum) than those children with severe muscular wasting and weakness.
3. Some infections were associated with a delayed recovery of the serum-protein pattern, but in 1 child the pattern continued to improve during a fever and a herpes simplex infection.
4. No particular pattern was associated with pellagroid skin changes.
5. The clinical outcome could not be foretold from a knowledge of the initial degree of depletion of serum albumin. The child in this series with the lowest serum albumin (1·0 g. per 100 ml.) recovered, whilst 3 others, in whom the initial serum-albumin concentration was higher, died.

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FORTHCOMING INTERNATIONAL MEDICAL CONFERENCES

The Third World Congress of Psychiatry will be held in Montreal, Canada, on 4 - 10 June 1961 under the auspices of the Canadian Psychiatric Association and McGill University. The official languages of the Congress are English, French, German, and Spanish.

The scientific programme will consist of plenary sessions, general sessions, panel discussions, symposia, and film sessions. In place of a single theme a number of functional approaches have been planned for the grouping of presentations. These are: Phenomenological or observational; experimental, including therapeutic; and interpretive or theoretical. Among the subjects of special interest are: addiction, alcoholism, animal behaviour, anthropology, biochemistry, child psychiatry, clinical psychology, clinical psychiatry, communication, constitution, development, electronic models — data processing, epilepsy, ethology, existentialism, family psychiatry, forensic psychiatry, genetics, geriatrics, group behaviour, hypnosis, juvenile delinquency, learning theory, mental hospitals, mental retardation, neurophysiology, neuroses, phenomenology, physical therapies, psychoanalysis, psychoses, psychoendocrinology, psychopharmacology, psychotherapy, psychosomatics, psychosurgery, psychopathological art, psychotomimetic drugs, religion and psychiatry, sleep and dreams, social psychiatry, social psychology, social therapies and after-care, and undergraduate and postgraduate teaching.

Applications to present papers or films must reach the Organizing Committee before 1 December 1960. Applications for registration must reach the Committee before 15 January 1961. Application forms, information about the programme, registration, accommodation, travel, etc. may be obtained from: Third World Congress of Psychiatry, Allan Memorial Institute, 1025 Pine Avenue West, Montreal 2, Canada.

VAN DIE REDAKSIE : EDITORIAL

ASMA

Die woord ‚asma' beteken vir die pasiënt fluitende asemhaling van welke oorsaak ook al. Die allergoloog sien dit as brongospasme as gevolg van 'n spesifieke hipersensitiwiteitsreaksie. Die psigiater is geneig om dit as 'n psigosomatiese siekte te beskou. Ons onderskei ook nog kardiale asma waar longedeem met brongospasme gepaard gaan.

Die woordjie ‚brongospasme' kan egter onder 'n vergrootglas geplaas word. As ons in kliniese sin praat van brongospasme, bedoel ons dat ons rongusse hoor, en lei daarvan af dat daar vernouing van brongusse en/of brongiole is, hetsy die gevolg van swelling van die slymvlies of spasme van die spierwand van die brongus. Daar word egter twyfel gewerp op die bestaan van ware spasme van brongiale spiere, en dit is veral onder torakale chirurge dat hierdie twyfel sterk op die voorgrond kom. Gilfillan[1] het twaalf pasiënte tydens segmentele longreseksie vir tuberkulose bestudeer. Die helfte het 'n geskiedenis van brongospasme gehad. Die brongiolêre bewegings is met 'n handlens bestudeer tydens operasie en ook 'n paar histologiese studies van brongiole is gedoen. Daar was geen spierhipertrofie in die asmalyers se brongiole nie. Vanuit 'n ander rigting het Wells[2] die probleem benader deur die meganika van asemhaling tydens asma-aanvalle te bestudeer. Die inspiratoriese en ekspiratoriese weerstand van die lugweg is albei vermeerder en na terapie is daar dikwels 'n groter verbetering in die inspiratoriese weerstand as in die ekspiratoriese weerstand. Dit weerspreek die opvatting van verhoogde ekspiratoriese weerstand as die hooffaktor in brongiale asma. Die werk van asemhaling is baie verhoog in asma, en dit is die geval byna uitsluitlik as gevolg van werk om lugweg-weerstand te oorkom. Hierdie bevindings sou meer ten gunste van edeem en afsluiting van brongusse deur afskeidings wees, hoewel brongospasme nie uitgesluit is nie.

So dikwels is mense met brongitis geneig tot asma aanvalle, veral in die winter, dat waar 'n geskiedenis van asma na 'n episode van infeksie van die boonste lugweg plaasvind, mens kan praat van brongitiese asma. Die dramatiese gevolge van antibiotiese terapie ter verligting van hierdie asma kan miskien ook gesien word as 'n verbetering van die lugweerstand deur afskeiding en edeem te verminder eerder as die opheffing van spierspasme om die brongusse. Geensins wil mens die brongospastiese element wegpraat nie, maar die klem net verskuif na die belangrike rol van edeem van die slymvlies tydens so 'n aanval.

Dat daar veelvuldige faktore vir hierdie edeem van die slymvlies is, is welbekend. Die volgende is voorbeelde hiervan: vogretensie van allergie (soos die nasale slymvliesswelling van hooikoors), inflammatoriese edeem (soos reeds genoem), en langdurige hipoksie met verhoogde kapillêre deurlaatbaarheid. Die dramatiese effek van kortisoon kan miskien in hoofsaak die vermindering van inflammatoriese edeem beteken, terwyl hipertoniese glukose ook op hierdie edeem deur dehidrasie sy effek mag hê. Vogtige klimaatstoestande wat verdamping van vog belemmer, is nadelig terwyl droë klimaatsomstandighede voordelig mag wees.[3]

Die ‚honger' na lug, 'n primitiewe behoefte in mens en dier, kan selde sonder emosionele reaksie geskied. Vrees is dus sowel 'n gevolg as 'n oorsaak van asma.[3] Die pogings van die pasiënt om lug deur hierdie vernoude buisie te stoot teen 'n hoër tempo verg meer werk en dus verdere uitputting, 'n groter behoefte aan suurstof vir spierwerking, en 'n verergering van die edeem as gevolg van hipoksie.

Waar onlangse werk dus meer die klem op die edeem en swelling van die brongiale slymvlies as op spasme van brongiale spiere laat val, moet mens miskien ook dienooreenkomstig jou begrip van asma effens wysig.

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RHEUMATOID ARTHRITIS

Steroid therapy in rheumatoid arthritis was first instituted about ten years ago by Hench *et al.*[1,2] at the Mayo Clinic. During these years many investigations have been carried out on the use of the adrenocortical steroids and their synthetic analogues in this disease, and there is now a fair understanding of the indications and contra-indications for the use of these potent agents. How they produce their beneficial effects is still virtually unexplained. Their benefits are only palliative or suppressive, not curative. They need to be given for an indefinite period, and there is always the risk of side-effects occurring, some of which are serious. Some patients become relatively refractory to these drugs after prolonged administration. The progress of the rheumatic process may not be halted, even when symptomatic relief is being maintained. In view of these difficulties certain policies have been adopted for the employment of the steroids. An authoritative review of this subject has recently been published by Boland.[3]

Steroid therapy should only be used in carefully selected cases where there is active and potentially reversible disease. Conservative treatment should first be employed, especially in mild disease with good chances of natural reversal. The optimum dosage for selected patients is an individual matter; and complete inhibition of the disease should not generally be sought. In discontinuing steroid therapy, the drug should not be abruptly withdrawn, but the dosage should be reduced gradually. Certain emergency conditions, such as severe infections, surgical operations, or injuries, necessitate the administration of additional amounts to cope with the stress.

Reports in the literature indicate great variations in the success obtained with cortisone and hydrocortisone therapy. It would appear that adequate improvement has been maintained in more than fifty per cent of patients. Variable results are to be expected in a disease such as rheumatoid arthritis, with its varying severity and with the various

schedules of dosage used in its management. The most frequent reason for inferior results has been the development of side-reactions. During the past five years synthetic steroid analogues have been tested. Of the hundreds that have been examined only a few have been marketed.

In 1954 prednisone and prednisolone became available. These drugs are more potent in anti-inflammatory activity than the natural hormones, and their administration does not lead to an increase in electrolyte activity. They are capable of producing improvement in patients no longer satisfactorily controlled by hydrocortisone or cortisone. The general incidence of side-reactions is essentially the same as with hydrocortisone, with a difference in the proclivity to induce certain effects. They are more prone to produce peptic ulcers and cutaneous ecchymoses, but less prone to cause salt and water retention and a rise in blood pressure.

Triamcinolone was manufactured in 1956. It is peculiarly liable to produce anorexia, muscle weakness, nausea, fatigue, and erythema. Methylprednisolone is satisfactory in antirheumatic activity, but would not appear to have advantages or disadvantages when compared with prednisolone. Its potency is somewhat greater.

The latest steroid whose therapeutic efficiency has been tested is dexamethasone.[3,4] The general incidence of untoward reactions with this antirheumatic drug is essentially the same as with prednisolone when comparable doses are given. Relatively common side-effects are excessive weight gain and ecchymotic skin lesions. This drug also has ulcerogenic properties, as revealed by routine radiographic studies of the upper gastro-intestinal tract.

The ideal suppressive agent for rheumatoid arthritis remains to be found. Great advances have of course been made, and better steroids may still be produced. There is of course always the possibility that some other type of chemical compound, or indeed some other type of treatment, may yet be found.

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FUNCTIONING ISLET-CELL TUMOURS OF THE PANCREAS

A REPORT ON TWO CASES

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The first functioning islet-cell tumour was recorded by Wilder in 1927.[1] In 1950 Howard reviewed 264 cases;[2] 200 of these were diagnosed during life and underwent surgery, 159 (79·5%) being relieved of symptoms. In the following 8 years 93 additional cases of functioning tumours were described.[3] The following are the case reports of 2 patients whom we have treated successfully:

Case 1

M.S., a 40-year-old European housewife, was first admitted to Groote Schuur Hospital in January 1959 with symptoms dating from July 1957, at a time when she had lost 30 lb. by dieting.

During these 18 months she frequently awoke between 4 and 6 a.m. in a confused state. At first she was aware that she was confused but later had no recollection of what happened. Her husband kept a diary in which he recorded her behaviour. Sometimes she woke up with a vacant stare, but this usually cleared up rapidly. At other times her behaviour during attacks was repetitive — her right hand jerked, she scratched her head, rubbed her nose, and twitched her eyelids. Unintelligible mumbles and spontaneous laughter frequently burst forth. Occasionally she saw double. Most times she sweated.

At the beginning (i.e. in July 1957) she was only mildly confused. Early in the course of her illness she was unable to write down her grocery order when required — 'I would take the pencil in my hand and my mind would go blank.' She found it difficult to light a cigarette — sometimes striking it on the match box. On one occasion she completely lost consciousness. She had a generalized epileptiform seizure about 6 months after her first episode of confusion and had 4 further seizures during the next 2 years.

Only once did an attack of confusion occur after breakfast; on this particular day she became confused and saw double at 4 p.m. and again at 10 p.m. while at a cinema. Attacks were more frequent premenstrually and during menstruation. A busy day in town was often followed by an attack the next morning. The episodes usually occurred 2 or 3 times a week. Early in the course of her illness she was symptom-free for 3 months. Later she had symptom-free periods of 2 - 3 weeks. During this time she was in the habit of taking a sweetened drink in the middle of the night as a prophylactic measure, having observed that her attacks were terminated by this means. She had now gained 30 lb. in weight.

Repeated estimations showed fasting blood-sugar levels which were often below 40 mg. per 100 ml., e.g. in July 1958 the level was 35 mg. per 100 ml., in January 1959 it was 97, in February 1959, 40, and in February 1960, 40, 57, 70, 41, 33, and 59.

The patient left hospital in February 1959 after 2½ weeks in bed in hospital during which time she was symptomless. She was readmitted in February 1960. At home she had been repeatedly drowsy in the early mornings, but again there were times when she was completely free of attacks for as long as 1 month. During her second hospital admission she was drowsy on most mornings before breakfast. She recovered each time rapidly after taking glucose by mouth.

Blood-sugar levels during the attacks ranged between 30 - 70 mg. per 100 ml. On 2 occasions she was comatose and could be resuscitated only by the administration of intravenous glucose. During one coma her blood-sugar level was 70 mg. per 100 ml., yet it was often under 45 mg. per 100 ml. when she was only mildly confused.

Physical examination was negative. There was no evidence of hepatic, endocrine, or gastro-intestinal disturbance. Liver-function tests were normal.

Case 2

J.D., a 38-year-old European housewife, was admitted to Groote Schuur Hospital on 19 March 1960 with a letter from her doctor requesting removal of an islet-cell tumour.

For 5 months before admission her husband noticed that she behaved peculiarly, usually at about 4 - 5 in the morning.

She woke up confused and dizzy, as though she was drunk, and talked nonsense. During these episodes she noticed an inability to concentrate, and she was very forgetful. She had visual hallucinations, frequently complaining that stars were shining from her chest. On one occasion she became violent and struck her daughter. Consciousness was never lost, although on recovery she was completely unaware of what had happened. She never perspired and there was no diplopia. Her husband had noticed that these episodes were always relieved by food and in order to forestall them he used to get up at 3 a.m. to make coffee. She had about one or two attacks weekly, but there was one period of complete remission for a month.

On examination there were no abnormal physical findings.

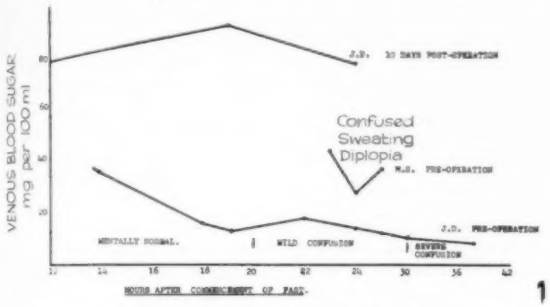

Fig. 1. Blood-sugar levels after prolonged fast.

Hypoglycaemia was confirmed following a fast (Fig. 1). During the fast her mental state was normal for the first 18 hours, and venous blood-sugar levels of 36 and 16 mg. per 100 ml. were recorded. She then became mildly confused, but was quite capable of conversing in spite of venous blood-sugar levels varying between 9 - 18 mg. per 100 ml.

It was only after 36 hours of fast that she became really drowsy and even then she could answer simple questions in monosyllables. A normal mental state was rapidly restored by the administration of 50 g. of glucose intravenously.

OPERATIONS

A liberal right paramedian incision is usually adequate and was used in both our patients. In both cases, the body of the pancreas was fully exposed, the tail was mobilized together with the spleen so that it could be lifted out of its bed, and the head of the gland was fully mobilized so that it could be brought forward with the duodenum and the termination of the common bile duct. The entire gland could, therefore, be carefully palpated between the fingers and thumb. In neither case was it considered justifiable to 'unhook' the uncinate process from behind the mesenteric vessels, but the gastrosplenic ligament, the gastrocolic omentum and the retroperitoneal connective tissues were thoroughly explored for possible out-lying tumours.

Case 1 (M.S.)

The tumour was fortunately detected during the initial exposure of the body of the pancreas. A small pinkish nodule, 0·5 cm. in diameter, could be seen projecting from the superior border of the neck of the pancreas where it merged with the neighbouring connective tissue surrounding the left gastric vein. On palpation the nodule was obviously much larger, measuring 1·5 cm. in diameter, and extended into the substance of the pancreas (Fig. 2). (Subsequent pathological examination showed that the visible part was a lymph node.)

Fig. 2. Hemi-pancreas (case 1). The arrow indicates the tumour on [illegible] the superior border of the neck.

On dissection it soon became obvious that the tumour was not well encapsulated, and this, together with its adherence to surrounding structures, suggested the possibility of malignancy, but there were no signs of glandular or other metastases and no further nodules could be seen or felt in the remainder of the pancreas. Nevertheless, distal pancreatectomy was performed after the gland had been mobilized, to a point 2 cm. beyond the tumour.

Blood sugar-levels were estimated at frequent intervals during surgery (Fig. 3). She was on a continuous 5% intravenous

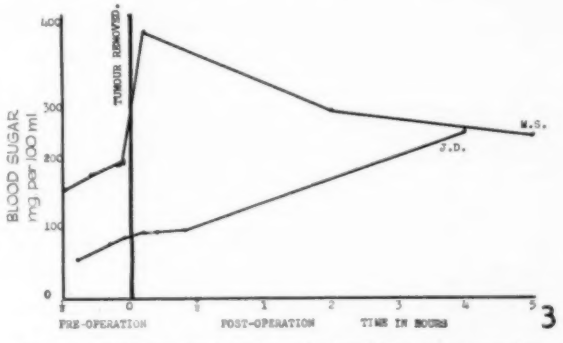

Fig. 3. Blood-sugar levels during and immediately after operation. A 5% solution of dextrose was given as a continuous infusion to M.S. (case 1), but was only given 2 hours after the operation to J.D. (case 2).

glucose drip. Handling the tumour had no effect on blood sugar, but immediate elevation followed its removal.

The *histology* of the nodule was that of an islet-cell tumour of the pancreas. It was not encapsulated. There was a great deal of fibrosis indicating that it had been present for some

time. It was a very vascular tumour with islet cells in close relationship to the vascular spaces. An intravascular tumour was clearly evident. The lymph node was congested but not invaded by tumour and the remainder of the excised pancreas was normal.

The *postoperative course* was uneventful. Glycosuria (up to ++++) persisted for 3 days and blood sugar levels were abnormally high for 2 days after surgery (220 and 185 mg. per 100 ml.). During this time she received nothing orally, but was given a continuous infusion of 5% glucose intravenously. There was pyrexia (up to 101°F.) for 4 days following surgery. Two weeks after surgery the fasting blood-sugar levels on 3 consecutive days were 104, 79 and 99 mg. per 100 ml. There were no hypoglycaemic symptoms during the 3 months following surgery.

Case 2 (J.D.)

No tumour could be found in the fully exposed and mobilized body and tail of the pancreas. After the head of the gland had been elevated forwards with the duodenum, a nodule 1·5 cm. in diameter was felt between the fingers and thumb, situated within the substance of the pancreas at about the centre of its head. This nodule could not be seen until the overlying peritoneum and pancreatic tissue had been incised. Then it appeared as a well defined pinkish tumour (Fig. 4). A plane of cleavage was developed between the

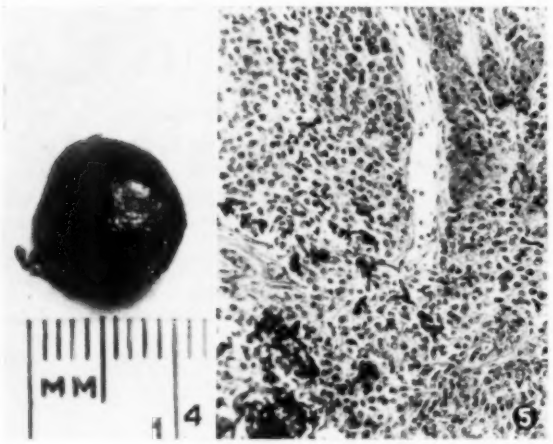

Fig. 4. Enucleated tumour (case 2).
Fig. 5. Tumour histology (case 2). (× 10)

tumour and the surrounding pancreatic tissue, and the adenoma was enucleated from its bed which was closed with fine silk mattress sutures. No other nodules could be detected and there were no signs of metastases. Handling the tumour did not affect the blood-sugar level. There was no appreciable rise in blood sugar 15 minutes after the tumour had been removed (Fig. 3), although 4 hours after removal the blood sugar had risen to 173 mg. per 100 ml. However, at this time the patient was receiving an infusion of 5% dextrose intravenously.

Histological examination (Fig. 5) showed a non-encapsulated islet-cell tumour composed of large cells with large, and often hyperchromatic, nuclei, presenting as small cords and islands of cells. Mitotic figures could not be found and vascular invasion was not observed.

The postoperative course was uneventful. Mild (+) glycosuria was noted only on the first 2 postoperative days. A pyrexia, never exceeding 100°F, persisted for 3 days. There have been no hypoglycaemic episodes during the 2 weeks since surgery. Two weeks after surgery a 24-hour fast was undertaken (Fig. 1). At the end of this fast the blood-sugar level was 79 mg. per 100 ml.

DISCUSSION

Both patients had symptoms of hyperinsulinism which were frequently induced by exercise or fasting, their fasting blood-sugar levels were repeatedly below 50 mg. per 100 ml., and both experienced dramatic relief after the administration of dextrose. They therefore satisfied the triad described by Whipple[4] which has been considered pathognomonic of insulinoma (although there have been 6 proved cases of insulinoma with fasting blood-sugar levels above 50 mg. per 100 ml.[2]).

The commonest cause of hypoglycaemic attacks is 'functional hypoglycaemia'.[5] The aetiology of this condition is incompletely understood, but is believed to be due to an abnormal and increased response by insulin-producing cells to a rise in blood sugar. Attacks characteristically occur 2 - 4 hours after meals and not in the fasting state.

Rarer causes of hypoglycaemia include gastro-intestinal malabsorption, hepatic, neurological, adrenal, and pituitary dysfunction — none of which were suggested in these 2 patients.

The comparative lack of correlation between venous blood-sugar levels and the state of consciousness in our patients is interesting and was also noted by Monro[6] in his patient, and by Porter and Frantz.[7] This has also been seen in insulin shock therapy.[8] The first patient was in coma on one occasion with a blood-sugar level of 70 mg. per 100 ml. She was unable to swallow fluids and true hypoglycaemic coma was proved by an absence of response to intravenous distilled water and an immediate improvement after 50 g. of dextrose. On occasions she was only mildly confused with fasting blood-sugar levels below 40 mg. per 100 ml.

The second case was even more remarkable. During a prolonged fast she was only mildly confused and quite capable of conversing, when venous blood-sugar levels were repeatedly recorded below 18 mg. per 100 ml. There was no evidence of any mental impairment when the blood-sugar level was 36 mg. per 100 ml. There is thus no doubt that if a patient with suspected insulinoma is subjected to a fast the blood-sugar levels should be estimated, since clinical assessment alone is inadequate. The blood samples were venous and this may explain why mental symptoms were not more prominent at these levels. Arterial and capillary blood-sugar levels might probably have been higher.

The increase in the blood-sugar level following surgery (nearly 200 mg. per 100 ml.) corresponds to that described by McMillan[9] and de Peyster and Gilchrist.[10] However, as far as we are aware the rapidity with which this occurs has not been stressed. McMillan reports the increase as occurring within 30 minutes of removing the tumour and others have observed it within 1½ - 4 hours. It would seem remarkable that the increased amounts of circulating insulin can be inactivated in 5 minutes. The biological half-life of exogenous insulin was found to be 24 minutes by radio-active methods.[11]

There are not many reports of serial blood-sugar estimations during surgery for insulinoma. A marked elevation such as occurred in case 1 must indicate that all functioning tumour tissue has been removed. This is important since a second functioning tumour exists

in 10% of cases. The second tumour may be extremely difficult to find, especially if situated in the head of the pancreas where it is often deep-seated.[12]

In our second case there was no immediate increase in the blood-sugar level after excision of the tumour. The presence of a second tumour was therefore suspected but not seen at surgery. Four hours after surgery the blood-sugar level had risen from 90 mg. per 100 ml. to 267 mg. per 100 ml. The patient was then receiving 5% dextrose intravenously and had had a total of 200 ml. by the time of the second reading. However, we feel that the increase is more than could be accounted for by the administration of dextrose. Fasting blood-sugar levels one week after surgery were normal, and we failed to produce hypoglycaemia after a 24-hour fast. It would seem therefore that the only functioning adenoma had been removed and that elevation of the blood-sugar level following surgery is not always immediate.

Unfortunately we were unable to assay the levels of insulin-like substances in the plasma in these cases. These substances have been shown to be very high with functioning islet-cell tumours[13,14] and they return to normal after successful removal of the tumour. There have, however, been cases of functioning islet-cell tumours with normal plasma-insulin levels.[15] In some cases spontaneous hypoglycaemia may be very difficult to demonstrate and, in these, Fraser advocates employing the insulin-tolerance test.[16] With insulinomas there is a slow return from hypoglycaemia. He states that the test is free from hazard if 3-hourly meals are ensured for the rest of the day and, in addition, he gives 50 mg. of cortisone if hypoglycaemia has been severe.

Hyperglycaemia and glycosuria are common following surgery and may persist for 1 - 10 days.[7] This occurred in case 1, but was not a feature of case 2.

In the reviews of Frantz[3] of 398 cases of insulinoma 78·6% were benign and 2 - 3 cm. in size. Of his cases 9·3% were definitely neoplastic with metastases which were usually present in the liver and regional lymph glands, but which, in some cases, were widespread. The remainder (12·1%) formed a group designated 'suspiciously malignant tumours'. Venous invasion and cytological evidence of malignancy are the most important histological evidence of the metastasizing capacity of these tumours. In our first case there was evidence of venous invasion. After a 10-year follow-up only 1 patient with this doubtful histological picture had a local recurrence with return of symptoms.[3] In view of the relative frequency of second tumours which may only manifest themselves clinically years later, this is probably no reflection on the histological findings. Secondary deposits have never been reported in this 'suspiciously malignant' group.

Symptom-free periods lasting up to 3 months occurred in our patients. Remissions for as long as a year have been reported.[17]

Pre-operative preparation with steroids has been advocated for 2 reasons. They increase blood sugar and they may possibly prevent postoperative hyperthermia, which is of unknown aetiology, but has been recorded as a cause of death.[2]

Surgery may involve no more than simple enucleation of a benign superficial lesion. If the tumour is malignant or deep-seated its removal may necessitate distal pancreatectomy, pancreato-duodenectomy, or even total pancreatectomy.[6,18] The fatality rate for the removal of an insulinoma was quoted as 16% in 1935,[19] but it is now considerably less. If no tumour is found the accepted procedure is a partial pancreatectomy with removal of the tail and half the body. As tumours are more or less evenly distributed throughout the gland there is approximately a 50% success rate following this operation.

SUMMARY

Two functioning tumours of the islets of Langerhans are described. Both patients had symptoms in the early morning while fasting. Both patients had remissions of symptoms lasting at least a month during the course of the illness. A lack of correlation between the clinical condition and level of blood sugar was evident in both cases. The rise in the blood-sugar level following surgery in both cases is considered to be a useful indication that all abnormal functioning tissue has been removed. Histological classification and its bearing on prognosis is discussed.

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HYPERTENSION IN UNILATERAL KIDNEY DISEASE: A SHORT DISCUSSION AND PRESENTATION OF CASES*

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The death rate from hypertension in the USA has been quoted as being 4 times that of cancer and 20 times that of diabetes mellitus or tuberculosis. The surgical treatment to date is empirical and medical treatment is difficult and requires constant supervision. The recognition, therefore, of hypertension due to unilateral kidney disease† is of importance, for this form of hypertension is often curable if dealt with in the early stages.

The classical work of Goldblatt and others (1934) showed the close association between unilateral renal ischaemia and hypertension, and since then the subject has been opened up by a number of publications, some of which are included in the bibliography. The mechanism of unilateral renal ischaemia as a cause of hypertension is not clearly understood, but something instrumental in increasing blood pressure is elaborated or produced by the ischaemic kidney and this pressor substance has been isolated from both normal and ischaemic renal tissue. It is thought to be a proteolytic ferment, renin, which acts on a globulin substrate in the plasma to produce a powerful pressor agent termed angiotonin, hypertensin (Braun-Menéndez) or now, by mutual agreement, angiotensin, and this substrate has been determined and synthesized. A great deal of experimental work has been done on the renin-angiotensin system but, although not fully understood, the mechanism is thought to be active in the acute stage of the hypertensive process that may follow a unilateral renal injury, but to almost disappear after the chronic stage has become established.

It is all-important in hypertension from unilateral disease that the treatment should be instituted as early as possible and before the chronic irreversible stage develops.

We have confirmed the clinical features in the successful cases quoted by Perera and Haelig. The onset is usually relatively abrupt in a subject previously normotensive, but there are a few cases in which the condition was preceded by benign essential hypertension. The disease tends to run a severe rapid course and to develop into the malignant phase. The onset may be marked by headaches, progressing rapidly to frank encephalopathy and retinopathy with visual disturbances and grave changes in the retinal artery. Later, general involvement develops, with albuminuria and a rapid drop in kidney function. The disease may begin at any age, but an onset before 20 or after 45 is highly suggestive, because essential hypertension is not commonly seen at these ages. The condition may be precipitated by trauma to the renal region, whether accidental or surgical. In embolism or thrombosis of the renal artery there is often a history of an acute attack of pain in the flank or lower abdomen and renal colic or appendicitis may be simulated. So a history of hypertension, developing within a few days of an injury or in an illness in a subject known to have had normal blood pressure, is important.

When these cases are investigated the renal function tests are usually not of help, for the function of the good kidney is usually temporarily reduced by the hypertension. *Intravenous pyelography* is sometimes helpful and it should, if possible, be carried out. A small renal shadow on one side is important; a fainter shadow on one side suggests reduced circulation or impaired tubular function, and failure of the intravenous pyelogram to visualize the pelvis of the kidney, which later yields a normal retrograde pyelogram, strongly points to an obstruction in the renal artery. However, normal pyelograms are frequently obtained with serious unilateral disease.

Differential renal-function tests by means of bilateral ureteral catheterization, so well described by Howard and his associates, are useful investigations. A diminished volume of urine, together with a lower concentration of sodium from one kidney in specimens taken simultaneously, is highly significant, and a reduction in the volume of urine of at least 50% and a reduction in sodium concentration of at least 15% as compared with the opposite kidney predicts a favourable outcome from surgery. The most dependable single investigation is aortography‡ and this procedure we have found practical and the risk involved relatively slight. Poutasse and Dustan (1956) believe that it is indicated in the following groups of patients with hypertension:

1. Those with unexplained disparity of size or function of the kidneys as shown by intravenous pyelography.
2. Young patients with no family history of hypertension and no apparent cause for it.
3. Elderly patients with sudden onset of accelerated hypertension.
4. Patients with essential hypertension, whose disease suddenly accelerates, especially when this acceleration follows an attack of unexplained pain in the flank.

Lipo-protein studies have been found of use in cases of atherosclerosis and have in a number of cases predicted to some degree what has later been demonstrated by aortography.

CASE REPORTS

Case 1

Y.H., aged 9 years. This girl was first seen on 16 August 1952 as an urgent case presenting with recurring convulsions, which required control by general anaesthesia on 2 occasions and by continuous deep sedation.

The mother reported that the girl was healthy until 18 months previously, and that since then she often woke up with a headache, suffered recurring attacks of nausea and vomited occasionally, but attended school until the day before the first convulsion.

On examination. A pale, very ill-looking child. Fundi showed grade-4 eye changes. Blood pressure 250/180 mm.Hg. Femoral pulses present and equal. Heart not clinically enlarged. Heart sounds closed with a marked accentuation of the aortic

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† See Editorial 'Narrowing of the renal artery', *S. Afr. Med. J.*, 6 February 1960 (**34**, 110).

‡ See article by Drs. Denny and Tinker on page 852 of this issue of the *Journal*.

second sound. No clinical evidence of an abdominal tumour. Urine: + albumin; centrifuged specimen showed numerous red cells, an occasional leucocyte, and no casts. Alkaline phosphatase 11·4 units %, inorganic phosphate 3·0 mg.%, serum calcium 8·7 mg.%, blood urea 45 mg.%, blood creatinine 0·8 mg.%. Benzodioxane intravenous test negative. Before this child was referred, an intravenous pyelogram had revealed some doubtful flattening of the upper calyx of the right kidney, but a retrograde pyelogram done immediately afterwards was reported to be within normal limits. X-ray of the wrists and ankles showed no evidence of renal rickets. The child's condition deteriorated 36 hours after admission and she developed a large retinal haemorrhage in the right eye.

Treatment. Although the prognosis appeared to be hopeless and because a definite diagnosis of the cause of the hypertension could not be made, it was decided to attempt a combined Smithwick operation and suprarenalectomy as a last resort. This was performed by Mr. Lee McGregor in two stages at an interval of 10 days. The right side was done first and following this the blood pressure dropped to 170/150 mm.Hg, and the child's condition improved; and soon after the second stage she improved rapidly and the blood pressure stabilized at about 120/90 mm.Hg and was easily controlled by replacement cortisone therapy. Her general condition improved daily and 2 weeks after the second stage the fundi had resolved entirely, the urine was free of albumin and the patient was able to leave hospital.

Pathological report on kidney biopsies showed nephrosclerosis of the hypertensive type.

23 September 1953. Enjoying good health on a maintenance dose of cortisone, 5 mg. twice a day. Tonsils successfully removed in August 1953. Recovered from whooping cough and measles without complications. Fundi normal. Blood pressure 120/88 mm.Hg. Urine concentration test, specific gravity 1020. Urine dilution test, specific gravity 1006.

30 September 1957, when aged 14 years. On maintenance cortisone, 5 mg. twice a day, and keeping very well. Healthy looking, but a little undersized. Normally developed. Fundi within normal limits. Blood pressure 140/90 mm.Hg. Pubic hair scanty. Heart not enlarged on screen examination. ECG within normal limits. Urine contained ? trace of albumin. Blood urea 28 mg.%. Electrolyte studies within normal limits. Intravenous pyelogram showed a compensatory hypertrophy of the right kidney and a small left kidney with some blunting of the calyces; the renal parenchyma was narrowed, measuring about 1 inch, and the appearance was suggestive of an old pyelonephritic kidney.

25 April 1958. Very well on cortisone, 5 mg. twice a day. Blood pressure 135/90 mm.Hg. Fundi within normal limits. Urine contained a trace of albumin. Nephrogram (Dr. M. Denny) showed a contracted left kidney with poor arterial supply. Normal right kidney. Selective ureteral catheterization (Mr. D. Venn): right kidney normal; left kidney low urea excretion, low volume, albumin ++, and no excretion of dye on the p.s.b. test. Left-sided nephrectomy advised.

2 September 1958. Left-sided nephrectomy (Mr. N. G. C. Gane, Salisbury). Pathological report: generally contracted chronic pyelonephritic kidney.

January 1959. Well-proportioned, normal pubic and axillary hair, no acne, menstruating regularly and normally, blood pressure 135/90 mm.Hg, urine albumin-free. Marked pigmentation of the nipples; no other pigmentation. Leads a full life, plays all games and is popular with the boys and a keen exponent of 'jive' and 'rock-and-roll'.

Review of case. The cause of the original hypertension is considered to have been a left-sided pyelonephritis.

Case 2

Mr. R.W.F., aged 59 years, postmaster. Seen on 6 December 1954, this patient complained of severe headaches for the previous 7 months, with progressive tiredness and attacks of irritability, and for the last 2 months a sudden progressive deterioration in vision.

Past health (record obtained from his family doctor). Had always been a healthy subject; served in World War II, but was boarded out on return from Abyssinia as a case of ? peptic ulcer. 1952, healthy (blood pressure 128/78 mm.Hg). 1953, blood pressure 160/90 mm.Hg. May 1954, blood pressure 190/110 mm.Hg. October 1954, seen by an eye specialist, who reported retinal haemorrhages.

On examination. A well-built man. Fundi showed grade-4 eye changes. Blood pressure when lying, 250/120 mm.Hg. Peripheral vessels not thickened; peripheral pulses all present and equal. Heart was not enlarged clinically. Heart sounds closed with a split second sound at the base. ECG showed left ventricular strain. Urine: Albumin +++; centrifuged urine showed moderate numbers of red cells, leucocytes, and hyaline and granular casts. Blood urea 36 mg.%. Blood count normal. Intravenous pyelogram showed poor function of the left kidney which was small, with some narrowing of the cortex. Aortogram within normal limits, but the nephrogram on the left side revealed poor vascularization, especially of the upper pole.

Treatment. 20 December, left-sided nephrectomy (Mr. C. Thompson). This was followed by an immediate drop in blood pressure to 130/90 mm.Hg. Three weeks after operation: blood pressure 150/90 mm.Hg, lying down; urine concentration test, specific gravity 1030; urine dilution test, specific gravity 1012; blood urea 40 mg.%.

Pathological report. Chronic pyelonephritic kidney.

Follow-up, June 1959. Has remained normotensive and is in normal health.

Case 3

Mr. H.M., aged 46 years. Seen on 29 December 1955, this patient had enjoyed good health and been normotensive until 9 months previously, when he began complaining of early morning headaches and progressive tiredness. His family doctor reported a sudden rise of blood pressure to about 180/110 mm.Hg, which 3 months later rose to about 200/140 mm.Hg and the patient was found to have albumin in the urine.

On examination. A well-built man. Fundi showed grade-1 eye changes. Peripheral vessels doubtfully thickened; all the peripheral pulses present and equal. Heart not enlarged clinically or on screen examination. Heart sounds closed and of good character. ECG within normal limits, except for tall T waves in the chest leads. Urine: Albumin ++++; centrifuged specimen showed 2 red cells per high-power field, together with epithelial cells and scanty leucocytes, and numerous hyaline casts and scanty granular casts; culture yielded a growth of *Staphylococcus albus.* Blood urea 42 mg.%. Blood creatinine 1·5 mg.%. Blood count within normal limits. Intravenous pyelogram: Right kidney shadow was faintly visualized, longitudinal measurement 3¼ inches; left kidney showed good dye excretion, longitudinal measurement 4¾ inches. Retrograde pyelogram: The shadow of pelvis and calyces of the right kidney were relatively small and disproportionately large in relation to the size of the renal outline, indicative of atrophy of the renal parenchyma; the left kidney was within normal limits.

The sudden onset of hypertension with albuminuria, a poorly secreting right kidney on intravenous pyelography, and the retrograde pyelogram findings, were considered to be consistent with the diagnosis of a right-sided chronic pyelonephritis and a nephrectomy was recommended.

4 January 1956. Right-sided nephrectomy (Mr. C. Thompson). Blood pressure on the morning of operation under preoperative sedation was 230/135 mm.Hg and immediately after operation it dropped to 115/80 mm.Hg. Three weeks later: Blood pressure 110/80 mm.Hg; urine — albumin ++, centrifuged specimen showed an occasional pus cell and an occasional hyaline cast but no red cells.

Pathological report. The kidney was reduced in size, the surface was finely granular, and the capsule was adherent. On section the cortex showed irregular atrophy. The kidney showed the histological features of chronic pyelonephritis.

3 months after nephrectomy. In good health. Blood pressure about 135/90 mm.Hg. Urine free from albumin.

October 1957. Not so well. Complained of renewed tiredness. Normotensive. Urine clear.

2 February 1958. Referred for reassessment. Complained of progressive tiredness, but no effort dyspnoea or effort angina.

TABLE I. CASES 1 - 6

Age, Sex	*BP*	*Presenting symptoms*	*IV Pyelogram*	*Aortogram*	*Lesion*	*Treatment*	*Follow-up*
9 yrs female	250/180	18 months—early morning headaches, nausea, vomiting 1 week—convulsions	L kidney—small, contracted	L kidney—small, poor blood supply	L kidney—chronic pyelonephritis	20.8.53—bilateral thoracolumbar sympathectomy 2.9.58—L nephrectomy	7 yrs: BP 130/90 mm. Hg, excellent health on cortisone 5 mg. *b.d.*
59 yrs male	250/120	7 months—severe headaches, deterioration in vision	L kidney—small poor function	L kidney—poor vascularization, especially the upper pole	L kidney—chronic pyelonephritis	L nephrectomy	5 yrs: BP 150/90 mm.Hg. normal health
46 yrs male 29.12.55	200/140	9 months—early morning headaches progressive tiredness	R kidney—poor concentration, smaller than left	nil	R kidney—chronic pyelonephritis	4.1.56—R nephrectomy	1½ yrs: BP 135/90 mm.Hg. good health
2.2.58	140/90	Progressive tiredness	nil	Aorta atherosclerotic L common iliac and R superficial femoral occluded	Atherosclerosis	Diet, anticoagulants, nicotinic acid	4 yrs: Normotensive, improved
54 yrs male	200/120	Sudden vertigo, temporary paralysis of L arm and L leg for 10 minutes	Normal	R nephrogram—normal L nephrogram—faint filling Aorta atherosclerotic	Atherosclerosis. ?? atherosclerotic stricture of left renal artery	Diet, anticoagulants, nicotinic acid	1 yr: BP 160/100 mm.Hg, improved
49 yrs female	230/150	6 months—severe headaches with vomiting Progressive loss of energy	R kidney—normal L kidney—ptosed, poor function	R kidney—renal artery, small saccular aneurysm L kidney—poor visualization	Polycythaemia vera with renal thrombotic incidents	Radio-active phosphorus	1½ yrs: Normotensive, good health, blood count normal
32 yrs male	130/85	Examination for old inactive bilharzia	R kidney—normal L kidney—?? right upper calyx	nil	Treated bilharzia	nil	5 yrs: Normal BP, good health
38 yrs	180/90	Headaches, tiredness	L kidney—one large cyst	nil	Congenital cysts (4)	Surgical removal	6 yrs: Normotensive
41 yrs	240/160	Ill, severe headaches	Both kidneys—polycystic disease	nil	Congenital polycystic disease	nil	9 yrs: Grave hypertensive renal disease

On clinical examination: Fundi within normal limits; in right arm radial pulse absent and blood pressure not recordable; left arm blood pressure 135/90 mm.Hg; heart not clinically enlarged; heart sounds closed and of good character; resting ECG within normal limits; effort ECG no change; pulses present in the right leg, but left femoral and left pedal pulses absent. *Aortogram:* Abdominal aorta grossly atherosclerotic and the outline irregular; marked narrowing of the origin of the right common iliac; left common iliac completely occluded from its origin to the commencement of the superficial femoral artery; good collateral circulation to the left leg by way of the gluteal vessels and the lumbar collaterals; right femoral artery occluded from the origin of the profunda femoris to the commencement of the adductor canal, and collateral circulation carried *via* the muscular branches of the profunda femoris and the re-formation of the femoral artery below the adductor canal; the popliteal vessels and the terminal vessels of the lower limbs filled normally. *Lipoprotein partition:* Total cholesterol 250 mg.%; beta lipoprotein cholesterol percentage 83; cholesterol phospholipid ratio 1·01.

Diagnosis: The patient was considered to be atherosclerotic with occlusive vascular disease of both legs.

Progress report. 21 February 1959. On a low-fat, low-cholesterol diet, supplemented with vitamin A, and with anticoagulant treatment, the patient has been keeping well and symptom-free.

Final review. This patient is considered to have been initially a case of unilateral chronic pyelonephritis causing hypertension, which was relieved by nephrectomy; and with later development of atherosclerotic disease with occlusive thrombotic disease in several sites and symptomatic improvement on a low-fat, low-cholesterol diet and anticoagulant treatment.

Case 4

Mr. K.M.F., aged 54 years, electrical engineer. Seen on 3 June 1958, this man had always enjoyed good health until 3 weeks previously, when he experienced a sudden attack of giddiness and paralysis of the left arm and left leg, which passed off in about 10 minutes. He was attended by his family doctor, who found that his systolic blood pressure was 220 mm.Hg. and venesected about 1 pint of blood, but the systolic blood pressure remained raised at about 210 mm. After this he continued working and appeared to be reasonably well, but walking fast for 200 yards brought on a cramp in the left leg which was immediately relieved by rest.

On examination. A muscular well-built man. Fundi were within normal limits. Peripheral vessels thickened, but not tortuous. In left leg femoral and pedal pulses absent. Blood pressure 200/120 mm.Hg. Heart not enlarged on screen examination. Heart sounds closed and of good character. ECG within normal limits. Urine: Free of albumin and sugar; centrifuged urine shows nothing of note. Blood count was within normal limits. Lipoprotein partition studies: Total cholesterol 336 mg.%; beta lipoprotein cholesterol percentage 81; cholesterol phospholipid ratio 1·11. Intravenous pyelogram showed normal function and no abnormality of note. Biological and chemical tests for catecholamines negative.

Aortogram: Right nephrogram was within normal limits. In spite of three injections, only faint filling of the left renal artery was obtained, and at no time was an adequate nephrographic phase shown. The lower aorta was arteriosclerotic and narrowed, and the origin of both common iliacs showed a similar change, the left being more marked than the right. The left internal iliac artery was occluded. The presence of atherosclerotic disease involving the aorta, and particularly the left common iliac artery, suggested a strong possibility that this process had extended up the left lateral wall of the aorta and was possibly involving the left renal orifice. In view of this, it was decided to have differential ureteric excretion studies undertaken.

Differential ureteric excretion. Right kidney: Volume 13·1 ml., urea 1·04 g.%, sodium 1·05 mEq. Left kidney: Volume 16·7 ml., urea 0·94 g.%, sodium 1·30 mEq. These studies showed no significant abnormality of function of either kidney.

Treatment. The patient was put on to a low-fat, low-cholesterol diet, supplemented with vitamin A (10,000 units

daily), intermittent heparin therapy (12,500 units a day intramuscularly for 8 weeks), and after this, oral anticoagulant treatment and nicotinic acid (1,000 mg. *t.d.s., p.c.*).

Present condition. The patient is doing a normal day's work. He is symptom-free, and has an average blood pressure of 160/100 mm.Hg. He is now due for a reassessment of his case.

General review. This patient is considered to be a case of atherosclerosis with aortographic evidence of atheroma involving the lower aorta, the vessels supplying the lower limbs, and possibly the left renal artery, the condition of which might have been clarified by selective catheterization. General symptomatic improvement, with a drop in blood pressure followed on medical treatment.

Case 5

Mrs. F.M.S., aged 49 years. This patient was first seen on 9 May 1958. She complained of recurring attacks of severe headache for some months, either frontal or occipital, and on occasions vomiting without relief of the headache; and of progressive loss of energy for 6 months. Before this illness she had enjoyed excellent health.

On examination. An anxious subject. Fundi within normal limits. Blood pressure about 230/150 mm.Hg. Peripheral vessels not thickened. Peripheral pulses present and equal. Heart not enlarged. Heart sounds closed and of good character. ECG within normal limits. Some tenderness over the right renal angle. Blood urea 30 mg.%. Chemical test for catecholamines negative. Blood count: Haemoglobin 19 g.%, PCV 59%; the blood picture was thought to be consistent with the diagnosis of commencing polycythaemia vera or a compensatory polycythaemia. Urine: Albumin, trace; centrifuged deposit showed presence of very scanty leucocytes; no epithelial cells, bacteria, red cells or casts. Urea clearance test, 40% of normal function. Intravenous pyelogram: Right kidney within normal limits; left kidney thought to be atrophied, with poor function.

Aortogram and nephrogram. Report: 'The right renal artery showed well-marked tortuosity, and a saccular aneurysm was seen arising from the lower division of the main renal artery just at its origin. In the left kidney at nephrographic stage a well-marked cortical blush was present, demonstrating the cortex of the left kidney, and at 10 minutes no excretion was seen from the left kidney. The findings were thought to be consistent with an aneurysm involving the right system, and possibly evidence of some atrophy of the left kidney as the result of chronic pyelonephritis'.

Progress. The patient was further observed and treated with hypotensive drugs, in particular serpasil and ansolysen by mouth, with very little progress. On 2 June 1958 the spleen became definitely palpable and a repeat blood count and blood-volume studies confirmed the diagnosis of polycythaemia vera. She was then treated with radio-active phosphorus and after a month's interval showed progressive improvement. In November 1958 she was symptom-free, blood pressure being about 140/100 mm.Hg, and the hypotensive drugs were discontinued. She continued to make progress and remained symptom-free, and has since been normotensive (average blood pressure 130/80 mm.Hg).

April 1959: Repeat intravenous pyelogram. Report: 'The spleen is much enlarged, and displaces the left kidney downwards. The calyceal outlines are not clearly demonstrated on the left side, but the concentration is sufficient to produce a dense shadow in the renal pelvis and upper part of the left ureter. The right kidney shows normal appearance.' At this time the haemoglobin was 13·1 g.% and the haematocrit 45%.

Summary and review. It is considered that this patient is a case of polycythaemia vera of insidious onset; and that before this became clinically obvious she developed renal thrombotic incidents, resulting in the Goldblatt phenomenon with a high blood pressure, which responded poorly to medical treatment until ultimately she became symptomatically well and clinically improved on therapy with radio-active phosphorus.

Case 6

Mr. R.W.C., aged 32 years, accountant. This patient was seen on 15 June 1950 when he was re-examined for bilharzia, which he had contracted when he was 14 years old and for which he had received 4 courses of treatment. At this re-examination a cystoscopy showed scattered bilharzial nodules indicative of old inactive bilharzia. At that time the intravenous pyelogram was normal except for one of the upper calyces in the left kidney, which was a little broadened and suggested the possibility of a slight abnormality in this kidney.

The patient remained well from July 1950 until early 1956, when he was referred as a case of high blood pressure of possible kidney origin, and in September 1956 a repeat intravenous pyelogram showed a large round tumour involving the upper calyces of the left kidney. At an exploratory operation of the left kidney a large cyst was found occupying most of the upper pole, and 3 smaller cysts lower down. The large cyst was enucleated and the small cysts were uprooted, leaving a healthy-looking kidney. After this operation the patient remained well and normotensive until February 1959, when he was reported to have a severe hypertension of 182/152 mm.Hg. A repeat intravenous pyelogram then showed evidence of a superficial mass projecting from the lower pole of the right kidney and minor changes in the pyelographic appearance of that kidney raised the suspicion of further small cysts within the renal substance. The left kidney showed evidence of generalized stretching and distortion of the calyces and a small crescentic calcification in the middle third of the kidney, and the renal pelvis filled poorly. Both kidneys showed evidence of some lobulation of the renal contours. The findings were considered to be consistent with bilateral polycystic disease of the kidneys.

Summary and review. This patient is considered to be a case of polycystic disease of the kidneys. This was difficult to diagnose clinically or on intravenous pyelogram in 1950, but 6 years later the intravenous pyelogram showed evidence of cysts involving the left kidney, and the hypertension was relieved by removal of the cysts, thus demonstrating the Goldblatt phenomenon. After a further interval of 3 years the hypertensive state returned, and the intravenous pyelogram then gave evidence of bilateral polycystic disease of the kidneys.

COMMENT

We have found that a careful history is helpful in selecting the cases which require detailed investigation, and the history of a known normotensive developing a sudden hypertension is useful. Most help has been obtained from aortography and by the differential kidney-function tests described by Howard and others. A successful outcome can only be decided by the result of surgery, which may consist of unilateral nephrectomy, endarterectomy of a renal artery, or a bypass graft to improve the renal circulation. These cases form a small fraction of all hypertensive patients, but in our experience they are definitely commoner than those due to phaeochromocytoma.

SUMMARY

The close association between unilateral renal ischaemia and hypertension, as reported by Goldblatt and others in 1934, and its diagnosis and treatment, are discussed. Stress is laid on the significance of sudden hypertension in a known normotensive subject.

Six case histories of hypertensive patients showing this feature are presented, 3 of them being cases of unilateral pyelonephritis successfully treated by nephrectomy. The other 3 cases are respectively (1) aortic atherosclerosis with a strong possibility of involvement of the left renal artery, (2) polycythaemia vera with renal complications, and (3) polycystic disease of the kidneys first involving the left kidney.

A tabular statement is also submitted of the chief features of these 6 cases.

Our thanks are due to colleagues who referred cases and who helped in the investigation of these cases. We are indebted to Dr. F. P. Reid for the notes on case 5 and to Messrs. H. C. Brayshaw and P. S. Olivier for the notes on case 6.

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RENAL ANGIOGRAPHY IN HYPERTENSIVE DISEASE*

M. B. M. DENNY, D.M.R. (LOND.) and A. J. TINKER, M.R.C.P. (EDIN.), *Johannesburg*

In the last decade aortography has become an increasingly popular method of investigation in cases of hypertension. It has, however, never achieved the degree of recognition and use which in the light of recent knowledge we know it to deserve. Two reasons for this are apparent, viz. (1) that many hypertensives were not restored to normal health after nephrectomy performed in the first flush of enthusiasm arising from Goldblatt's epoch-making experimental work,[1] and (2) that radiologists and other interested workers tried to read more into the radiographs than they really have to offer.

We refer specifically to the radiographic appearances in the pyelonephritic contracted kidney. We have learnt from experience, and Hodgson[2] has recently pointed out, that

* A paper presented at the 42nd South African Medical Congress (M.A.S.A.), East London, C.P., September - October 1959 (see article by Drs. Denny and Tinker on page 848 of this issue).

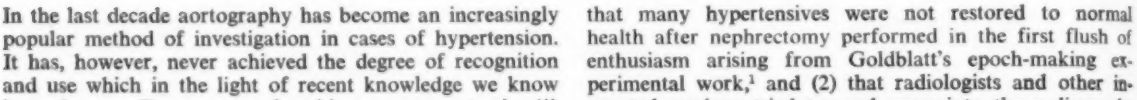

Fig. 1. Middle-aged man. Hypertension of sudden onset; 3 month's duration. Double kidney right side and slight foreshortening of inferior calyx of inferior pole.
Fig. 2. Same patient as in Fig 1. Arterial phase. Incomplete ramification of vessels to lower pole of right kidney.
Fig. 3. Negative defect of lower pole of right kidney in nephrographic phase. (Segmental resection with return of blood pressure to normal.)

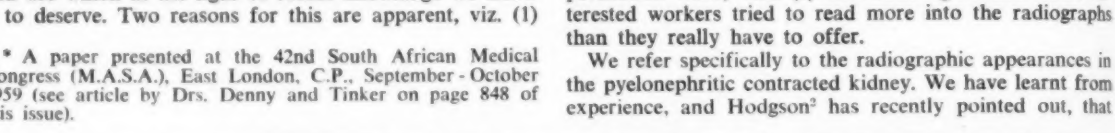

Fig. 4. Hypertensive aorta with inadequate filling of left renal artery.
Fig. 5. Selective catheterization of the left renal artery showing patent vessel.
Fig. 6. Aortogram with Somerville pump showing excellent opacification and developing stenosis in a mildly hypertensive female with obliterative peripheral vascular disease.

any attempt to detect abnormality in the interlobular and arcuate vessels is fruitless. With the means of radiography at present at our disposal it is clear that our efforts must be confined to the larger renal vessels. An exception is the negative defect in the nephrographic phase associated with a localized renal infarction (Figs. 1 - 3). Gellman[3] has clarified the position, and with his work and that of Poutasse[4] aortography has assumed its rightful place as a significant and important investigation.

We now accept that this examination is of positive value only when it demonstrates an inteference with the normal renal blood supply due to one of the many causes found in Gellman's published group of cases†.[3]

Hodgson[2] has indicated that a normal pyelogram may be obtained in the Goldblatt type of kidney where occlusion is not complete, and we have had similar experiences confirming this observation. It is clear, then, that within the confines of Gellman's criteria for aortography,[3] a normal pyelogram is no contra-indication to aortography, which should be proceeded with immediately.

As to the technique of aortography, the translumbar technique with its attendant dangers is definitely outmoded and redundant. Samuel and Denny[5] have already indicated this view and now, after 5 year's uninterrupted experience with the Seldinger technique,[6] we can reaffirm this opinion. The contrast medium — 76% urografin — which we have also used since 1955 without demonstrable ill effect on the kidneys, has recently been shown in an experimental study by Berg[7] to have no chemotoxic effect on the kidney in rabbits.

Our present technique is as follows:

We first catheterize the patient's femoral artery by the Seldinger method[6] and pass a 205 polythene catheter up to the level of the 2nd lumbar vertebra, using the Phillips 5-inch image intensifier to control the level. The catheter is rendered radiopaque by being filled with contrast medium, after which the proximal stopcock is turned off. A trial dose of 10 c.c. or less of contrast medium is then injected and a film is exposed, or the area is viewed through the intensifier, to ascertain whether there is evidence of filling of the commencement of the renal vessels. If so, a further 20 c.c. is injected by means of the Stirling pressure device,[8] producing a pressure of approximately 500 mm. of mercury. Three films are then rapidly exposed, the first immediately before the completion of the injection.

In some cases inadequate filling (Fig. 4) or no filling of one or other renal artery is noted; the cause of this may be either technical or pathological. Where the patient has a high blood pressure at the time of the investigation, the tremendous velocity of blood flow tends to sweep the dye away extremely rapidly and also enhances the 'streamlining' effect of flow, seen on occasions in normal individuals. This, together with a particular inclination of the catheter tip, may well produce an erroneous impression that the vessel is occluded. In cases like this we consider it pointless, and probably unwise, to persist with further attempts to opacify the vessel by the same technique, and we then turn to the green Kifa opaque catheter with its preformed curve. This catheter can be introduced immediately after the attempt with the Seldinger method, or it may be postponed for a day or two.

Should it be necessary to proceed with selective catheterization, there are 2 manœuvres for the introduction of the green Kifa catheter that can be used.

In the first of these, the 205 polythene catheter, already in the aorta, is withdrawn, with or without screen control, into the femoral artery, and the long 160 Seldinger guide wire[6] is passed through it into the aorta, leaving an extra-arterial length of wire greater than that of the polythene catheter. The catheter is then withdrawn and firm compression over the artery is exercised. The Kifa catheter is introduced into the aorta over the 160 wire, care being taken that the preformed curve is inclined at the site of the renal artery which one desires to fill. Edeling *et al*,[8] have recently indicated that with renal arterial catheterization there is a danger from a possible ischaemic effect produced on the kidney by the degree of obstruction which the catheter produces in the renal artery. Dr. E. Lipworth has also informed us that the Swedes consider that the dislodgement of an atheromatous plaque, with consequent renal arterial embolization, is a possibility.

We have found that in the cases in which it is necessary to perform a selective arterial catheterization, in any part of the aorta, it is not essential to place the catheter within the artery, but merely to approximate the tip of the catheter to the orifice of origin of the artery, preferably in an inferior position. Futhermore, we have never experienced arterial embolization, even in the most atherosclerotic arteries, when using the Seldinger 205 catheter. Our experience with the Kifa catheter is limited, but we see no reason why it should not be equally safe when carefully manipulated, for its resilience is almost equal to that of the 205 catheter.

With the catheter in position, a small test injection of 5 c.c. is made and the filling of the artery is confirmed on the angled intensification viewer. A further injection of 8 c.c. of 60% urografin is then made and a single 1-second exposure is executed immediately after the commencement of the injection (Fig. 5).

The second manœuvre that may be used is to insert the green Kifa catheter by repuncture of the opposite femoral artery, using the 205 cannular needle for this purpose.

One of us demonstrated the preparation of the opaque catheter at the Congress by means of a cinema film, and said, however:

It is as well to emphasize the necessity of a small second aperture 1 cm. proximal to the tip of the catheter. This aperture is angled towards the aortic wall and is on the superior and convex aspect of the catheter. The purpose is to ensure filling of the aorta at the point of origin of the renal artery. This is of particular importance if by any chance, probably during the injection, the tip of the catheter enters the renal artery. In such circumstances it is conceivable that a narrowed origin of the renal artery would otherwise be missed, in the absence of associated opacification of the adjacent aortic blood flow (Fig. 6). We have in recent months found that in using the Somerville pump with a pressure of 60 lb. per square inch through the reduction valve, an extremely rapid injection of contrast media (20 c.c.) can be made. The images of the aorta and the renal arteries are brilliant

† The indications are discussed in the article by Drs. Denny and Tinker on page 848 of this issue.

and, since the introduction of this method, we have not been obliged to resort to selective catheterization.

Another procedure of value in ensuring better filling of the renal artery is to reduce the blood pressure to near normal levels by medical means. To achieve this result Poutasse[4] uses intravenous arfonad before the injection. To further enhance the brilliance of the image and the adequacy of renal arterial filling, we now use general anaesthesia and find that fluothane in many instances reduces the blood pressure to, or almost to, half the pre-anaesthetic level.

Where the blood pressure is very high, an intravenous drip containing arfonad has quickly and satisfactorily reduced the pressure to half the pre-anaesthetic level. As soon as the desired level is obtained, the drip is stopped and the injection given. The blood pressure returns to its normal level within 15 minutes.

In conclusion we wish to emphasize how much the use of the image intensifier has facilitated the performance of this investigation. A 9-inch image intensifier and 35 mm. camera is now in use, and with some refinement of technique with respect to film speed, type, and development, it would appear that the whole nephrographic procedure will possibly be satisfactorily achieved on ciné film.

We wish to thank Dr. R. G. Sauer for permission to publish Figs. 1 - 3.

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THE EMOTIONAL PATTERN OF THE TRIBAL ZULU AS IT AFFECTS PRE-ANAESTHETIC ASSESSMENT AND MANAGEMENT*

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It is one of the implicit functions of an anaesthetist to note the emotional state of his patient in order to induce tranquility by means of reassurance, suggestion and suitable premedication. For the European anaesthetist some knowledge of the history, beliefs and customs of the Zulu, as presented in this paper, proves very rewarding, if not indispensable for success, when anaesthetizing the *apparently* complacent and robust average Zulu.

Certainly the tradition-bound tribal Zulu is a stoical person. Fear, however, is deceptively masked by the absence of its outward manifestations. Thus the usual reaction to stress can be described as autonomic rather than vocal. The Zulu shares the belief of other warrior races that courage, as such, should be regarded as a primary virtue, and any display of fear as contemptuous self-indulgence. The psychosomatic implications of this are the actually exaggerated responses anaesthetists encounter daily in the Zulu as a result of moderate physiological and pharmacological interference.

A clue towards the uniqueness of the Bantu in general, as a subject for anaesthesia, is undoubtedly his poor nutritional state, but that is by no means the whole story. Lamont and Blignault[1] found 18 cases of delirium tremens and 12 cases of alcoholic hallucinosis among 258 male Bantu admissions to Weskoppies (Mental) Hospital. They all cleared up completely in a short period, despite their lack of a balanced diet.

As a district surgeon for several years it was my duty to examine the Zulu inmates of a certain gaol who were sentenced to be flogged. I was invariably impressed by their nonchalant, even disdainful bearing. This calm exterior, however, belied an intense emotional reaction ascertainable from recordings of pulse-rate and blood pressure; these revealed gross sympathetic overactivity as a rule.

* Abstract of a paper read at a meeting of the Atherstonian Society, 12 November 1959, Entabeni Hospital, Durban.

I had no controls from other racial groups, but these cases completely changed my previously-held opinion of the Zulu as an unimaginative race with peculiarly stable autonomic nervous systems. More recently my experience as an anaesthetist has confirmed and strengthened this new view. Anaesthetists in other parts of the world appear to concur. Keating[2] reported an abnormally severe carbohydrate metabolic response to surgical trauma in coloured Jamaican patients, and attributed this to an excessive adrenal activity, adding that it might well account, in part, for 'the high operative mortality and circulatory collapse during or after severe surgical trauma in this racial group'. This observation is the lot of every anaesthetist I have known working at our enormous non-European hospital, however immune he may have imagined himself to 'cardiac arrests' before arrival here.

Poe,[3] of Memphis, Tennessee, states: 'The sharp difference between the mortality rates in White and Negro subjects has been noticed by many observers. There are several explanations. It has been said that the Negro is particularly susceptible to apprehension, fright and panic. The physiological symptoms which accompany the state of anxiety interfere with the anaesthesia management in these cases'. It is perhaps significant that the Zulu uses the special word *qataza* for excrement passed in extreme fear.[4] In days gone by epidemics of *qataza* are said to have affected entire villages when the execution parties of the old Zulu kings were in the neighbourhood. Many similar examples of abnormal parasympathetic predominance may still be seen today in country practice in Natal and Zululand. Especially familiar to general practitioners here is a syndrome of incapacitating psychosis associated with little or no organic demonstrable pathology, apparently induced by a witch doctor. Thus a common obsession is one of angry ancestral spirits desiring the death of the victim and, indeed actual death purely in deference to the *inyanga's*

predictions is considered commonplace. Dehydration and inanition may account for this, just as the typically listless, uncomplaining and fatalistic outlook certainly suggests schizophrenia, but to my mind all that still does not explain the exceptionally common concomitant evidence of excessive vagal tone.

Zulus from the country, and to a lesser extent those from the towns and cities, often hold the naïve view that the hospital is a place where people are sent to die. They are inordinately afraid of anaesthetic and surgical procedures, being commonly much less confident of a successful outcome than the better-informed European. The Zulu is particularly prone to attribute his illness to supernatural intervention, having an acute awareness of supernatural powers, of which he is invariably mortally afraid. This rarely applies, incidentally, to obvious aetiology such as trauma.

It should always be remembered that fortitude, dignity and lots of patience are national traits of the tribal Zulu, inculcated by an upbringing based on his natural customs and tradition. This should, however, never mislead one as necessarily implying a placid nature. On the contrary, anticipation of his nature as described above demands positive action on the part of the anaesthetist. Psychological preparation should always include a greeting and the articulate expression of a few readily learned courtesies in the Zulu language. After rapport with the patient has thus been established an interpreter may take over, to furnish a brief explanation of the purpose of the anaesthetic and the assurance (where reasonably justified) that all will be well. Great care should be taken not to patronize the adult patient unduly. The Zulu belongs to a tribe which rose to greatness on its own, inheritors of a truly great tradition.

Irrespective of whether local or general anaesthesia is in the offing, an effective dose of anticholinergic and sedative drug combination, such as full therapeutic doses of pethidine, promethazine, and perhaps atropine as well, should never be omitted from the premedication. Phenothiazine derivatives such as mepazine[5] (pacatal), perphenazine, chlorpromazine and promazine[6] have been found to afford specific protection to dogs against cyclopropane-adrenaline arrhythmias. Zulu patients should have the benefit of this, quite apart from our impression of the greater incidence of postoperative nausea and vomiting among non-Europeans. Otherwise I am convinced that analgesic solutions containing adrenaline, and cyclopropane-induced general anaesthesia, will result in disaster for the Zulu far more commonly than for the European or Asian.

While being guided in general by the condition of the individual patient, my preference, therefore, is for 'heavy' premedication. Unfortunately the malnutrition and accompanying disturbed liver-function must temper this tendency. With phenothiazine derivatives accurate timing of premedication is less important, another big advantage over atropine as a sole anticholinergic and antisialologue drug. I therefore consider the use of a phenothiazine derivative justified, despite the possibly slightly delayed recovery.

It may be mentioned in conclusion that, apart from these emotional factors, there is more than an inherently greater risk in the Zulu as a subject for anaesthesia. For instance, his greater incidence of pericarditis,[7] which is usually tuberculous in origin, of beri-beri heart disease, and probably of 'cardiac failure of unknown origin'[7] must always be borne in mind.

I wish to thank Prof. Sir R. Macintosh, of Oxford, and Dr. H. Grant-Whyte, Head of the Department of Anaesthesia at King Edward VIII Hospital, for encouragement and perusal of the manuscript, and Dr. J. W. Mostert, now of the Johannesburg General Hospital, for his help in the preparation of this abstract.

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THE EFFECT OF VARIOUS FORMS OF SUPPLEMENTATION ON THE NUTRITIVE VALUE OF MAIZE FOR CHILDREN*

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As a staple cereal food, maize is of particular importance in South Africa. It is the largest cereal crop in the Union and among rural populations 52 - 75% of human calorie consumption is derived from it.[1] The association of predominantly maize diets with a high incidence of kwashiorkor is well known both in Africa and in South and Central America.[2,3] Although an excellent source of calories, maize is deficient in niacin, vitamin B_{12}, vitamin C, folic acid, calcium, and sodium. The protein of maize is deficient in the 2 essential amino-acids, lysine and tryptophan, and the amino-acid leucine is present in excess. As a source of protein, maize has the further disadvantage that its total protein content is only 9%. This necessitates the consumption of a large daily quantity of maize to cover minimal daily protein requirements. A 25 lb.-child, for example, would need to eat ½ lb. of dry maize (approximately 60 - 70 oz. of porridge) to receive sufficient protein for growth and maintenance.

In the supplementation of maize all its deficiencies should be taken into account.[4] In this study the supplementation of maize with respect to its protein content in particular has been investigated. Mineral and vitamin supplements were provided for all children who were on the trial diets so that the nutritive value of the protein alone could be evaluated. Convalescent cases of kwashiorkor, aged 1 - 4 years, were used as test subjects 15 - 100 days after admission to hospital. Nutritive value was measured by means of 3-day nitrogen balance periods. Methods used were as previously described.[5]

Supplementation of maize with lysine and tryptophan. The synthetic amino-acids lysine and tryptophan were added to give a mean increase of 176 mg. per g. nitrogen of lysine and 47 mg. per g. nitrogen of tryptophan to maize protein. Nitrogen retention was significantly increased over that of unsupplemented maize protein. Although the utilization of maize protein is improved by synthetic amino-acid supplementation, its practical usefulness is limited if total protein intake cannot also be increased.

* Abstract of paper presented at Research Forum, University of Cape Town, 27 July 1960.

Supplementation of maize with pea flour (Pisum sativum var. arvense). A mixture of ⅔rds maize to ⅓rd pea-flour has a protein content of 14%. Feeding of this mixture resulted in nitrogen retentions equivalent to milk at intakes of protein above 2·5 g. per kg. per day. At intakes between 1·9 and 2·5 g. of protein per kg. per day, the nitrogen retentions were significantly less than that of an isonitrogenous milk diet and no better than an unsupplemented maize diet.

Supplementation of maize with pea flour and fish flour. A mixture made up in the following proportions — maize 60%, pea flour 30%, and fish flour 10% — has a protein content of 20%. Feeding of this mixture resulted in nitrogen retention that was not different from that of a pure milk diet at levels of protein intake both above and below 2·5 g. per kg. per day.

Supplementation of maize with pea flour and milk powder. A mixture made up in the following proportions — maize 60, pea flour 30, and skimmed milk powder 18 — has a protein content of 18%. Feeding of this mixture resulted in nitrogen retentions that were not different from that of a whole-milk diet at all levels of protein intake.

Conclusions

Vitamin, mineral, and protein requirements must all be taken into account when the supplementation of maize is contemplated. These studies have demonstrated that relatively small amounts of fish flour (10%) or milk powder (18 parts) need be added to a 2 : 1 maize/pea mixture to give a protein with a nutritive value not demonstrably different from that of whole-milk diet at all levels of protein intake. The practical implication of these findings is that among protein-deficient populations available supplies of animal protein such as milk, egg or fish flour can be stretched much further if combined in proper proportion with staple cereal or vegetable diets.

This work was carried out in the Clinical Nutrition Unit of the South African Council for Scientific and Industrial Research at the University of Cape Town. Special thanks are due to the Fishing Industries Research Institute, Cape Town, for the supply and analysis of the fish flour. Hind Brothers supplied the pea flour, and Vereeniging Consolidated Mills, the maize.

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L. M. Marchand
Medesekretaris

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It is a rule of the South African Medical and Dental Council that a medical practitioner may not accept any appointment unless it has been advertised in the public press and in the *South African Medical Journal*. Consequently the *Journal* cannot refuse to publish a professional advertisement submitted for publication. The appearance of an advertisement in the *Journal*, therefore, does not necessarily mean that the appointment which is advertised carries the approval of the Association.

In order to assist its members, however, the Association has adopted the procedure of investigating, through its Branches, the terms of service in connection with appointments for which advertisements are submitted for publication. If a Branch does not approve of an appointment a 'Warning Notice' is placed in a prominent position on one of the pages containing the professional advertisements in the same issue of the *Journal* as the advertisement appears. In this notice the particular appointment is mentioned and medical practitioners are advised to communicate with the Branch concerned (whose name is also given) before sending in their applications.

L. M. Marchand
Associate Secretary

Plaza Building
Pretoria
22 September 1960

43ste MEDIESE KONGRES (M.V.S.A.), KAAPSTAD, 24 - 30 SEPTEMBER 1961 : 43rd MEDICAL CONGRESS (M.A.S.A.), CAPE TOWN, 24 - 30 SEPTEMBER 1961

SCIENTIFIC EXHIBITIONS

A circular letter from the Chairman of the Scientific Exhibition Sub-Committee is reproduced below for the information of members of the Association:

'It it the intention of the Organizing Committee to arrange a scientific exhibition in conjunction with the proceedings of Congress. We feel that this will offer a unique opportunity for the demonstration of scientific research and other work presently being carried out in the Union, not only by official bodies and sponsored research units and groups, but also by individual doctors and scientists.

'The approach to this exhibition will be as broad as possible and will include anthropology and genetics, psychology and industrial aptitude testing, public health and sanitation, the medical applications of atomic energy, nutrition, food technology and quality control, therapeutic substances, production and control, health education and immunization procedures, veterinary work and the zoonoses, hospital planning and medical services administration, the history of medicine and its instruments, tribal medicine and customs, as well as the full field of medical research. General practitioners are included.

'One part of the exhibition will be a cinematograph theatre showing a daily programme of medical and scientific films, coloured slides, etc. It is hoped that closed-circuit television will be included.

'This preliminary circular is being sent to as many organizations and individuals as possible who may care to take part in the exhibits. To assist the planning committee, it would be appreciated if prospective exhibitions would indicate, as soon as possible, whether or not they or their organizations would be prepared to exhibit, and if so briefly indicate:

'1. The nature and title of the exhibit.

'2. Whether it will be (*a*) static display, (*b*) working demonstration, or (*c*) ciné or slide projection.
'3. Approximately what (*a*) linear, or (*b*) square footage of display space will be required.
'4. Whether power, water, drainage, or gas will be required.
'5. If films or slides are to be shown, the approximate time taken.

'After this information has been received, preliminary plans will be drawn up and a subsequent circular early in 1961 will deal with the detailed plans, arrangements for demonstrators, delivery and erection, insurance, etc.

H. O. Hofmeyr
Chairman, Scientific Exhibition Sub-Committee

Medical House
35 Wale Street
Cape Town
12 September 1960'

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Mr. B. A. Armitage and Dr. T. H. Whitsitt.

Northern Transvaal Branch
Dr. J. T. M. de Villiers, Prof. O. V. S. Kok, Drs. W. H. Lawrance, W. A. Lombard, J. H. Struthers, and P. N. Swanepoel.

O.F.S. and Basutoland Branch
Drs. J. Gilliland, R. Theron, G. F. C. Troskie, and J. W. van der Riet.

O.F.S. Goldfields Branch
Dr. F. N. Gillwald.

Southern Transvaal Branch
Drs. C. Adler, A. L. Agranat, B. T. Bernstein, J. I. H. Frootko, R. Geerling, E. T. Meyer, H. I. Osler, H. Penn, T. Radloff, F. W. Roberts, T. Schneider, M. Shapiro, and S. Spiro.

South-West Africa Branch
Dr. W. H. G. Kuschke.

Transkei Branch
Dr. E. R. Louw.

Vaal River Branch
Not yet elected.

UNIVERSITEITSNUUS : UNIVERSITY NEWS

UNIVERSITEIT VAN PRETORIA

By die Promosieplegtigheid op 10 September 1960, is die volgende grade in die geneeskunde toegeken:

Graad van Magister in Geneeskunde

Abouchabki, Anthony Raymond (Interne Geneeskunde).
Van der Westhuizen, Frans Willem (Obstetrie en Ginekologie).

Baccalaureus in Geneeskunde en Snykunde

Coetsee, Idalette Magdalena
Menge, Paul Hansen
Rink, Albert Paul
Van Schalkwyk, Herman Eben
Weilbach, Cecilianus Nool
Dussé, Ronald
Olivier, Roelof
Van der Werke, Irma Erna Anja
Wegerif, Rita

IN DIE VERBYGAAN : PASSING EVENTS

Lede word daaraan herinner dat hulle die Sekretaris van die Mediese Vereniging van Suid-Afrika, Posbus 643, Kaapstad, sowel as die Registrateur van die Suid-Afrikaanse Geneeskundige en Tandheelkundige Raad, Posbus 205, Pretoria, moet verwittig van enige adresverandering. Versuim hiervan beteken dat die *Tydskrif* nie afgelewer kan word nie. Dit het betrekking op lede wat oorsee gaan sowel as dié wat binne die Unie van adres verander.

* * *

Research Forum, University of Cape Town. The next meeting of Research Forum will be held on Wednesday 5 October at 12 noon in the Bennie de Wet Lecture Theatre, A-floor, Groote Schuur Hospital, Observatory, Cape. Prof. J. F. Brock will speak on 'Impressions of the Fifth International Nutrition Conference held in Washington'. All interested are invited to attend this meeting.

University of Cape Town and Association of Surgeons of South Africa (M.A.S.A.), Joint Lectures. The next lecture in this series will be held on Wednesday 5 October at 5.30 p.m. in the E-floor Lecture Theatre, Groote Schuur Hospital, Observatory, Cape. Mr. R. D. Casserley will speak on 'Intrathoracic cysts — pathology and management'. All members of the Medical Association are welcome to attend this lecture.

* * *

South African Society of Obstetricians and Gynaecologists (M.A.S.A.), Cape Town Sub-Group. At the Annual General Meeting of this Sub-Group held at Medical School, University of Cape Town, Observatory, Cape, on 14 September, the following office bearers were elected for the year 1960 - 1961: Chairman — Dr. F. N. Charnock; Hon. Secretary — Dr. Pierre du Toit; Committee members — Drs. R. Nel, L. Abramowitz and N. Louw.

Suid-Afrikaanse Vereniging van Verloskundiges en Ginekoloë (M.V.S.A.), Kaapstadse Sub-Groep. By die Algemene Jaarvergadering van hierdie Sub-Groep, gehou te Mediese Skool, Universiteit van Kaapstad, Observatory, Kp., op 14 September, is die volgende ampsdraers verkies vir die jaar 1960 - 1961: Voorsitter — dr. F. N. Charnock; Eresekretaris — dr. Pierre du Toit; Komiteelede — drs. R. Nel, L. Abramowitz en N. Louw.

* * *

Dr. D. K. Quinlan, M.B., B.Ch. (Rand), L.M. (Dubl.), Dip. O. & G. (Rand), F.C.O. and G. (S.A.), formerly senior lecturer in obstetrics and gynaecology at the University of Natal, has commenced practice as an obstetrician and gynaecologist at 819 Colonial Mutual Buildings, West Street, Durban. Telephones: rooms 21839, residence 857186, after hours 63737.

Dr. D. K. Quinlan, M.B., B.Ch. (Rand), L.M. (Dubl.), Dip. O. & G. (Rand), L.K.V. en G. (S.A.), voorheen senior lektor in verloskunde en ginekologie aan die Universiteit van Natal, het as verloskundige en ginekoloog begin praktiseer te Colonial Mutual-gebou 819, Wesstraat, Durban. Telefone: spreekkamer 21839, woning 857186, na ure 63737.

* * *

The Society for Clinical and Experimental Hypnosis, Northern Section, is considering running a course of instruction in hypnosis for doctors, dentists, and psychologists. Doctors who are interested in participating in this course should write to Dr. B. W. Levinson, c/o Tara Hospital, Hurlingham, Johannesburg.

* * *

Dr. Pauline Klenerman, of Durban, has recently returned from a visit to Europe, where she visited hospitals in London and also attended a meeting of the Medical Women's International Association in Baden-Baden, Germany.

IN MEMORIAM

HYMIE (CHAIM) IPP, M.P., B.CH. (RAND)

Dr. M. Arnold, of Johannesburg, writes:

Dr. Hymie (Chaim) Ipp died tragically on 2 July after being involved in a road accident the previous day.

Dr. Ipp qualified in Lithuania in 1938, *cum laude*. His wife qualified simultaneously. He became interested in dermatology and internal medicine under the influence of his uncle, the well-known dermatologist, Dr. Isaac Ipp.

Dr. H. Ipp

When Lithuania was occupied in 1941, Dr. Ipp and his wife were confined to the ghetto in Kaunas for 4 years, during which time they gave yeoman service to the community. After a dramatic escape, they made their way to Western Germany, where Dr. Ipp was put in charge of a hospital under American control. Subsequently the family emigrated to South Africa, where Dr. Ipp repeated his clinical training according to the requirements of the South African Medical and Dental Council. After serving as Senior Medical Officer at Edenvale Hospital, where he earned the respect and affection of his colleagues, he completed a postgraduate course in dermatology and medicine at the Johannesburg Hospital. He then took up his last post, as registrar at the King Edward VIII Hospital, Durban, where he impressed his colleagues with his great enthusiasm and ability.

VRAE BEANTWOORD : QUESTIONS ANSWERED

GENITAL MONILIASIS

Q—*Married couples often complain of repeated infections of the genitalia (diagnosed as moniliasis and other fungus infections). I have found the application of 'mycostatin' ointment and the use of 'mycostatin' pessaries extremely useful, but the effect of treatment seems to be temporary only. How should this problem be approached in order to achieve more lasting results?*

A—When repeated attacks of monilial vaginal infection occur the first consideration must be to exclude the possibility of sugar in the urine. As regards the local infection the causal fungus can be cultured and tested for sensitivity. As a rule one finds the organism is sensitive to 'mycostatin'. It is advisable, after the diagnosis is proved, to prescribe 'mycostatin' pessaries to be used twice daily for *2 weeks* instead of the 1 week's course usually advised. If this is done fewer cases relapse.

The usual advice concerning frequent changes of underclothing and meticulous local cleanliness should be given. Intercourse is prohibited until cure is established. In resistent cases nystatin can also be given by mouth and gentian violet pessaries used between antibiotic courses. A 'tampax' with the tip dipped in gentian violet is useful for self-treatment. Very occasionally infection with both monilia and trichomonas may be found together, and here the course of 'mycostatin' is best followed by a 6 weeks' continuous course of 'SVC' pessaries used twice daily.

Readers are invited to submit questions for this column to the Editor, *South African Medical Journal*, P.O. Box 643, Cape Town.

WORLD LIST OF FUTURE INTERNATIONAL MEETINGS

ALTERATIONS AND ADDITIONS NOTIFIED DURING AUGUST 1960

Symposium on Diagnosis and Treatment of Acute Radiation Sickness, Geneva, 17 - 22 October 1960. World Health Organization, Palais des Nations, Geneva, Switzerland.

World Health Organization, Study Group on *Poliomyelitis,* Geneva, 7 - 12 November 1960. Palais des Nations, Geneva, Switzerland.

World Health Organization, Conference on Research on Rehabilitation of *Leprosy* Patients, Vellore, India, 14 - 24 November 1960. Palais des Nations, Geneva, Switzerland.

International Symposium on the Etiology of Myocardial Infarction, Detroit, 16 - 18 November 1960. Dr. Thomas N. James, Chairman, Section on Cardiovascular Research, Henry Ford Hospital, Detroit, Michigan, USA.

Symposium on Diseases of the Liver, Brussels, 19 November 1960. Dr. O. Hoste, General Secretary, Colloquia on Gastroenterology, Gouden Handstraat 9, Bruges, Belgium.

International College of Surgeons, North American Federation, Annual Congress, Chicago, 7 - 11 May 1961. Dr. Horace E. Turner, International Secretary-General *pro tem.*, International College of Surgeons, 1516 Lake Shore Drive, Chicago 11, Illinois, USA.

NUWE PREPARATE EN TOESTELLE : NEW PREPARATIONS AND APPLIANCES

COMBIZYM

Newport Trading Corporation (Pty.) Ltd. announce the introduction of Combizym tablets, manufactured by Luitpold Werke, of Munich, Germany, and supply the following information:

Combizym tablets represent a novel approach to the treatment of gastro-enteric metabolic disturbances and their ensuing symptoms (dyspepsia, cachexia, flatulence, meteorism, hypoproteinism, etc.) by total enzyme substitution.

Combizym, a multivalent ferment compound, is composed of fungus (plant) and pancreatic enzymes (cellulase, amylase, protease, esterase, lipase, trypsin, pepsin) in a high and acid-resistant concentration which makes it eminently suited for the treatment of all types of indigestion or maldigestion of foods throughout the whole of the digestive tract. Its action starts in the stomach (acid medium) and continues through the duodenum and small and large intestines with an alkaline reaction (pancreatic enzyme part). The addition of lipase will compensate for bile-deficiency in cases where cholepathy is the responsible aetiological factor (idiopathic steatorrhoea). While remaining active in hypo- and hyperacid media, Combizym also takes over the functions — by way of substitution — of certain metabolic processes normally generated by the liver (bile) and pancreas — if and when respective pathological processes are involved (acute and chronic hepatopathies, pancreopathies). Combizym is thus an ideal enzyme treatment of the 'gastro-enteric syndrome' of a rather complex nature and origin (idiopathic, allergic, neural and pathological).

Combizym aims at the removal of the symptoms (flatulence, fullness, meteorism, etc.) and at the increased absorption of fats, proteins, and carbohydrates (also iron) through complete metabolic breakdown in the digestive tract.

Dosage. 1 - 2 (3) tablets swallowed whole with meals.

Further information and samples of Combizym will be supplied by the sole importers: Newport Trading Corporation (Pty.) Ltd., P.O. Box 1871, Johannesburg.

FERROMYN

Westdene Products (Pty.) Ltd. announce the introduction of Ferromyn, a modern concept of oral iron therapy from the research laboratories of Calmic Ltd., of England, and supply the following information:

Ferromyn is prepared from the mild atoxic ferrous salt of succinic acid and is now clinically established as the most effective organic iron salt. It requires no other additive to produce a rapid haemoglobin response or to reduce intolerance of side-effects usually associated with oral ferrous therapy. By virtue of its superior utilization and absorption, an increase of approximately 24% of haemoglobin can be obtained with Ferromyn only 17 days from the commencement of therapy.

Cope *et al.*[1] in a controlled clinical trial found Ferromyn taken orally to be as effective as intravenous and intramuscular iron in all but a few refractory cases, and they consider it the product of choice even for severe degrees of iron-deficiency anaemia. Furthermore, Ferromyn has a remarkably low incidence of intolerance. This incidence was reported by Gillespie[2] to be less than 1%. By virtue of its bland properties Ferromyn is particularly suitable for infants or children and for administration throughout the course of pregnancy.

Ferromyn is available in the form of capsules and as a palatable elixir. The average dosage is 1 capsule or 1 teaspoonful 3 times a day.

Further information may be obtained from the sole South African distributors, Westdene Products (Pty.) Ltd., P.O. Box 7710, Johannesburg.

1. Cope, E. *et al.* (1956): Brit. Med. J., **2**, 638.
2. Gillespie, R. M. (1955): Medical Illustrated, **9**, 147.

BOEKE ONTVANG : BOOKS RECEIVED

Henry E. Sigerist on the History of Medicine. Edited by Félix Martí-Ibáñez, M.D. Pp. xviii + 313. $6.75. New York: MD Publications, Inc. 1960.

Diseases of the Skin. By James Marshall, M.D. (Lond.). Pp. viii + 944. 496 illustrations. 84s. net plus 3s. 7d. postage abroad. Edinburgh: E. & S. Livingstone Ltd. 1960.

Synopsis of Opthalmology. By William H. Havener, B.A., M.D., M.S. (Optha.). Pp. 288. 189 illustrations. South African price £2 17s. 6d. Local agents: P. B. Mayer, P.O. Box 713, Cape Town. St. Louis: C. V. Mosby Co. 1960.

Synopsis of Treatment of Anorectal Disease. By Stuart T. Toss, M.D., F.A.C.S., F.I.C.S. Pp. 240. 59 illustrations. South African price: £2 15s. 3d. Local agents: P. B. Mayer, P. O. Box 713, Cape Town. St. Louis: C. V. Mosby Co. 1959.

Synopsis of Ear, Nose, and Throat Diseases. By Robert E. Ryan, B.S., M.D., M.S. (ALR), F.A.C.S.; William C. Thornell, A.B., B.M., M.D., M.S. (ALR), F.A.C.S. and Hans von Leden, M.D., F.A.C.S., F.I.C.S. Pp. 335. 59 illustrations. South African price: £2 17s. 6d. Local agents P. B. Mayer, P.O. Box 713, Cape Town. St. Louis: C. V. Mosby Co. 1959.

Synopsis of Gynecology. 5th edition. By R. J. Crossen, M.D.; D. W. Beacham, M.D. and W. D. Beacham, M.D. Pp. 340. 106 illustrations. South African price: £2 15s. 3d. Local agent: P. B. Mayer, P.O. Box 713, Cape Town. St. Louis: C. V. Mosby Co. 1960.

Microchemical Methods for Blood Analysis. By Wendell T. Caraway, Ph.D. Pp. xi + 109. 4 illustrations. 42s. Springfield: Charles C. Thomas. Oxford: Blackwell Scientific Publications Ltd. 1960.

Predisposition to Postvaccinial Encephalitis. Significance of Constitution, especially The Status Dysraphicus in the Genesis of Postvaccinial Encephalitis. By E. J. W. Keuter. Pp. 160. 46s. London: D. van Nostrand Company Ltd. (Distributors for Elsevier). 1960.

Gastric Cytology — Principles, Methods and Results. By R. O. K .Shade, M.D. (Dunelm), M.D. (Tübingen), L.R.C.P., M.R.C.S. Pp. viii + 81. 85 figures. 35s. net. London: Edward Arnold (Publishers) Ltd. 1960.

Therapeutic Radiology. By William T. Moss, M.D. Pp. 403. 146 illustrations. South African price: £5 6s. 3d. Local agent: P. B. Mayer, P.O. Box 713, Cape Town. St. Louis: C. V. Mosby Co. 1959.

Symposium on Glaucoma. Transactions of New Orleans Academy of Opthalmology. Edited by William B. Clarck, M.D., F.A.C.S. Pp. 313. 99 illustrations. South African price £5 14s. 9d. Local agent: P. B. Mayer, P.O. Box 713, Cape Town. St. Louis: C. V. Mosby Co. 1960.

BRIEWERUBRIEK : CORRESPONDENCE

MEDICAL AID SOCIETIES

To the Editor: The Border Branch of the Medical Association of South Africa has for some time been perturbed at the increasing chaos in medical practice caused by the high-handed unilateral action of the insurance companies underwriting medical aid societies. Repeated attempts to counteract this have been made by the Branch in the form of a public meeting and press statements.

It is therefore with extreme gratification that the Branch observes similar concern expressed by Drs. N. R. Pooler[1] and P. H. Dalgleish.[2] In view of the increasingly deteriorating doctor-patient relationship emanating from the above, this Branch resolved 'that Federal Council be requested to hold an immediate investigation into the relationship existing between

medical aid societies underwritten by insurance companies and the Medical Association of South Africa'.

J. R. van Heerden
Assistant Hon. Secretary
Border Branch (M.A.S.A.)
P.O. Box 405
East London
13 September 1960

1. Correspondence (1960): S. Afr. Med. J., **34**, 680.
2. *Idem* (1960): *Ibid.*, **34**, 796.

CEREBRO-CARDIAC SYNDROME

To the Editor: It was with great interest that I read Professor Brink's[1] annotation on the electrocardiographic study of the so-called cerebro-cardiac syndrome and his suggestion that the aetiological factor in the ventricular dysrythmia was possibly subendocardial haemorrhages.

In an analysis, some time ago, of the extracranial pathology associated with severe head injuries in a series of 400 fatal cases, subendocardial haemorrhages were found in 102, subepicardial haemorrhages in 15, 'fatty' changes in 3, and other pathology (adherent pericardium, old infarction, patent foramen ovale, and syphilis) in 18. Congestion, oedema, and 'ballooning' of the lungs were common findings, but evidence of direct bruising was rare. The outstanding pathological feature in the cardiac pathology was the presence of subendocardial haemorrhages. Their occurrence ranged from one or two small isolated petechiae to large diffuse subendocardial ecchymoses, often extending into the papillary muscles. Invariably the left ventricle only was involved; in one case only was another chamber, the right auricle, affected.

Subepicardial haemorrhages were often associated findings, but in a number of cases they occurred alone, again confined to the left ventricle only. Their aetiology is probably asphyxial, but it is noteworthy that not only did they occur in cases of almost instantaneous deaths, but they were frequently seen in patients who died days afterwards. Presumably, in patients who survive for a longer period, absorption takes place with subsequent fatty changes in the myocardium, giving rise to the flabby musculature so frequently seen.

Routine electrocardiographic examinations should be more frequently carried out in severe head injuries, and we have frequently come across bizarre, but usually transient, findings.

In the case presented by Professor Brink the injury appears to be more of a focal nature, since the patient appears to have been dazed only. Whether the haemorrhages discussed above could occur under these circumstances is open to considerable conjecture. One is likewise sceptical of the occurrence of abnormal electrocardiographic changes attributable directly to craniocerebral conditions in the absence of local cardiac pathology.

Incidentally, I am somewhat surprised that an air encephalogram was carried out so soon — 3 days — after the injury. We even refrain from carrying out a 'diagnostic' lumbar puncture at so early a stage, especially in the presence of a possible space-occupying lesion.

D. A. Muskat, Dip. Med., Ch.M.
504 Medical Arts Building
Jeppe Street
Johannesburg
14 September 1960

1. Brink, A. J. (1960): S. Afr. Med. J., **34**, 727.

POLELA ASSOCIATION

To the Editor: This letter is being written by a layman to draw the attention of medical officers to the Polela Health Centre.

It is assumed that most are familiar with the origin and development of the Health Centre and readers wishing to gain further information are referred to the following articles:

1. Gear, H. S. (1943): S. Afr. Med. J., **17**, 167.
2. Kark, E. and Kark, S. L. (1945): Clin. Proc., **4**, 284.
3. Kark, S. L. (1942): S. Afr. Med. J., **16**, 197.
4. *Idem* (1944): *Ibid.*, **18**, 39.
5. *Idem*. *In* Cluver, E. H., ed. (1951): *Social Medicine*, p. 661. Cape Town: Central News Agency.
6. Kark, S. L. and Cassel, J. (1952): S. Afr. Med. J., **26**, 101, 132.

Brief mention need only be made here of the type of work undertaken and facilities available.

Since 1940 Polela has functioned as a clinical and educational centre for the treatment of disease and for health education. Local cooperation with the community and educational and agricultural authorities has been achieved. A general service for the treatment of the sick has been provided as well as an epidemic service for neighbouring districts.

Family health and medical care has meant the provision of a health programme for a population of some 10,000 people in approximately 1,000 homes in an 'intensive area', besides a semi-intensive service which has been provided at subcentres outside the main area.

A skilled team of medical officers, nurses, health assistants, medical aides, and nursing aides has been trained since the inception of the Centre. Polela has built up a reputation throughout the Western world for its work in an underdeveloped area.

Since World War II Polela has been used by the University of Natal's Departments of Education, Psychology, and Economics for research work and, apart from numerous studies by medical officers at the Centre, a wide variety of research in many fields has been conducted by the above Departments. A highly skilled staff conversant with local practices and concepts, together with the exceptionally cordial relations enjoyed by the Centre with African residents in the area, has meant that in the past research workers have been able to undertake extensive programmes without the delays and frustrations so often associated with this type of enquiry.

Polela and its environs provided the University of Natal and other research workers from overseas with a laboratory for the social sciences not easily found elsewhere in Africa. Besides many articles on research work in social medicine, the Health Centre can boast of publications stemming from work at Polela in psychological, anthropological, educational, and sociological journals. The University has at present a number of projects on hand which it wishes to implement with the aid of the local Polela staff.

At present, however, the Health Centre is labouring under an acute shortage of medical staff. There is only one medical officer and work at the former high productive level can no longer be carried out. In order to popularize the work of this Centre, and in the hope that medical officers will again be drawn to this type of work, which offers tremendous opportunities, a Polela Association has been formed to draw attention of medical officers in South Africa and overseas to the work of Polela.

Further enquiries should be addressed to: The Polela Association, c/o University of Natal, P.O. Box 375, Pietermaritzburg.

P. D. Hey, M.A., Ph.D.
University of Natal
P.O. Box 375
Pietermaritzburg
9 September 1960

SANSOM

To the Editor: The administration of claims by this Company is reasonably up to date and it is only in cases where the information at our disposal is not sufficient and where we require further information that delays still occur in the settlement of claims.

It would appear that there are still some policy-holders who do not send in their claims to the Company when they receive their account from the doctor. If a policy-holder postpones submitting his claim, there is a delay for which the Company cannot be held responsible. Where such cases occur, the Company usually gets the blame.

It would help us considerably if doctors would make a note on their accounts to the effect that it is the first, second, third, etc. account. If we then receive a claim form with an account other than the first account, we can write to the policy-holder and request him to submit his claims at an earlier date. In this way it should be possible for us to ensure that accounts are submitted earlier.

G. H. Hansmann
Managing Director
South African National Sickness
and Accident Insurance Co. Ltd.
P.O. Box 1
Sanlamhof, C.P.
21 September 1960